

NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

RELATED APPLICATIONS

This application claims priority from USSN 60/186,592, filed March 3, 2000; USSN 60/186,718, filed March 3, 2000; USSN 60/187,293, filed March 6, 2000; USSN 60/187,294, filed March 6, 2000; USSN 60/190,400, filed March 17, 2000; ; USSN 60/196,018, filed April 7, 2000; USSN 60/259,548, filed January 3, 2001; each of which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

The invention relates generally to polynucleotides and polypeptides, as well as vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides.

SUMMARY OF THE INVENTION

The invention is based in part upon the discovery of novel nucleic acid sequences encoding novel polypeptides. The disclosed FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6 and FCTR7 nucleic acids and polypeptides encoded therefrom, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as "FCTR" nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated FCTR nucleic acid molecule encoding a FCTR polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In some embodiments, the FCTR nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a FCTR nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a FCTR polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that

includes the nucleic acid sequence of any of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a FCTR_X nucleic acid (*e.g.*, SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24) or a complement of said oligonucleotide.

Also included in the invention are substantially purified FCTR_X polypeptides (SEQ ID NO: 2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25). In certain embodiments, the FCTR_X polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human FCTR_X polypeptide.

The invention also features antibodies that immunoselectively-binds to FCTR_X polypeptides, or fragments, homologs, analogs or derivatives thereof.

In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, *e.g.*, a FCTR_X nucleic acid, a FCTR_X polypeptide, or an antibody specific for a FCTR_X polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a FCTR_X nucleic acid, under conditions allowing for expression of the FCTR_X polypeptide encoded by the DNA. If desired, the FCTR_X polypeptide can then be recovered.

In another aspect, the invention includes a method of detecting the presence of a FCTR_X polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the FCTR_X polypeptide within the sample.

The invention also includes methods to identify specific cell or tissue types based on their expression of a FCTR_X.

Also included in the invention is a method of detecting the presence of a FCTR_X nucleic acid molecule in a sample by contacting the sample with a FCTR_X nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a FCTR_X nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a FCTR_X polypeptide by contacting a cell sample that includes the FCTR_X polypeptide with a

compound that binds to the FCTR_X polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, *e.g.*, a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, Turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bücklers corneal dystrophy. The Therapeutic can be, *e.g.*, a FCTR_X nucleic acid, a FCTR_X polypeptide, or a FCTR_X-specific antibody, or biologically-active derivatives or fragments thereof.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast

adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The method includes contacting a test compound with a FCTR_X polypeptide and determining if the test compound binds to said FCTR_X polypeptide. Binding of the test compound to the FCTR_X polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy,

demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy by administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a FCTR_X nucleic acid. Expression or activity of FCTR_X polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses FCTR_X polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of FCTR_X polypeptide in both the test animal and the control animal is compared. A change in the activity of FCTR_X polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a FCTR_X polypeptide, a FCTR_X nucleic acid, or both, in a subject (*e.g.*, a human subject). The method includes measuring the amount of the FCTR_X polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the FCTR_X polypeptide present in a control sample. An alteration in the level of the FCTR_X polypeptide in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell

mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a FCTR_X polypeptide, a FCTR_X nucleic acid, or a FCTR_X-specific antibody to a subject (*e.g.*, a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome,

liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

5 In yet another aspect, the invention can be used in a method to identify the cellular receptors and downstream effectors of the invention by any one of a number of techniques commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

10 Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present
15 specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION

20 The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The novel nucleic acids and their encoded polypeptides are referred to individually as FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6, and FCTR7. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "FCTR".

The novel FCTR nucleic acids of the invention include the nucleic acids whose
25 sequences are provided in Tables 1A, 2A, 3A, 3C, 3E, 3F, 3G, 3H, 4A, 5A, 5C, 5E, 6A, 6C, and 7A inclusive ("Tables 1A - 7A"), or a fragment, derivative, analog or homolog thereof. The novel FCTR proteins of the invention include the protein fragments whose sequences are provided in Tables 1B, 2B, 3B, 3I, 4B, 5B, 5D, 6B, 6D, and 7B inclusive ("Tables 1B - 7B"). The individual FCTR nucleic acids and proteins are described below. Within the scope of this
30 invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

FCTR1

Novel FCTR1 is a growth factor ("FCTR") protein related to follistatin-like gene, and mac25. FCTR1 (also referred to by proprietary accession number 58092213.0.36) is a full-length clone of 771 nucleotides, including the entire coding sequence of a 105 amino acid protein from nucleotides 438 to 753. The clone was originally obtained from thyroid gland, kidney, fetal kidney, and spleen tissues.

The nucleotide sequence of FCTR1 as presently determined is reported in Table 1A. The start and stop codons are bolded and the 5' and 3' untranslated regions are underlined.

Table 1A. FCTR1 nucleotide sequence (SEQ ID NO:1).

GGTCCTCACCCCTTCCTCTCTCCAGCCTCGGTGCTGTTACGGCTCCTCTGCTCGCATTGTGACTTTGGGCCAGGCTGGGGGA
AATGACCCGGGAGGGTCCCATGCGGCTACATAAAATTGGCAGCCTTAGAACTAGTGGGAAGGCGGGTGC CGGAAGTCGAGGGGCGG
AGAGAGGGGGCCGGAGGAGCTGCTTTCTGAATCCAAGTTCGTGGGCTCTCTCAGAAGTCCTCAGGACGGAGCAGAGGTGGCCGGCG
GGCCCGGCTGACTGCGCCTCTGCTTTCTTCCATAACCTTTCTTTCCGACTCGAATCACGGCTGCTGCGAAGGGTCTAGTTCGGG
ACACTAGGGCCCCAGATCGTGTACATCCATATGACACTTGGGAATGTGACAGGGCAGGATGTGATCTTTGGCTGTGAAGTGTGTC
CTACCCCATGGCCTCCATCGAGTGGAGGAAGGATGGCTTGGACATCCAGCTGCCAGGGGATGACCCCCACATCTCTGTGCAGTTTA
GGGGTGGACCCAGAGGTTTGAGGTGACTGGCTGGCTGCAGATCCAGGCTGTGCGTCCCAGTGATGAGGGCACTTACCGCTGCCTT
GCCCGCAATGCCCTGGGTCAAGTGGAGGCCCTGCTAGCTTGACAGTGCTCACACCTGACCAGCTGAACTCTACAGGCATCCCCCA
GCTGCGATCACTAAACCTGGTTCTGAGGAGGAGGCTGAGAGTGAAGAGAATGACGATTACTACTAGGTCCAGAGCTCTGGCC

The predicted amino acid sequence of FCTR1 protein corresponding to the foregoing nucleotide sequence is reported in Table 1B. FCTR1 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the cytoplasm (certainty=0.6500) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR1 protein is 11711.8 daltons.

Table 1B. Encoded FCTR1 protein sequence (SEQ ID NO:2).

MASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQLR
SLNLVPEEEAESEENDYY

FCTR1 was initially identified with a TblastN analysis of a proprietary sequence file for a follistatin-like probe or homolog which was run against the Genomic Daily Files made available by GenBank. A proprietary software program (GenScan™) was used to further predict the nucleic acid sequence and the selection of exons. The resulting sequences were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length protein.

In an analysis of sequence databases, it was found, for example, that the FCTR1 nucleic acid sequence has 31/71 bases (43%) identical and 46/71 bases positively alike to a *Mus Musculus* IGFBP-like protein (TREMBL Accession Number:BAA21725) shown in Table 1C. In all BLAST alignments herein, the "E-value" or "Expect" value is a numeric indication of the probability that the aligned sequences could have achieved their similarity to the BLAST query

sequence by chance alone within the database that was searched. For example, as shown in Table 1C, the probability that the subject ("Sbjct") retrieved from FCTR1 BLAST analysis, in this case the *Mus Musculus* IGFBP-like protein, matched the Query FCTR1 sequence purely by chance is 1.2×10^{-11} .

5 Table 1C. BLASTP of FCTR1 against *Mus Musculus* IGFBP-like protein (SEQ ID NO:38)

PTNR:REMTREMBL-ACC:BAA21725 IGFBP-LIKE PROTEIN - MUS MUSCULUS (MOUSE), 270 AA.
LENGTH = 270

SCORE = 161 (56.7 BITS), EXPECT = 1.2×10^{-11} , P = 1.2×10^{-11}
IDENTITIES = 31/71 (43%), POSITIVES = 46/71 (64%)

QUERY: 9 DGLDIQLPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPAS 68
+||+ +|||| +|+|| |||| | | | + | +| ||| | | | ||+|+ ++ +
15 SBJCT: 191 EGLE-ELPGDHVNIQVQVGGPSDHETTSWILINPLRKEDEGVYHCHAANAIGEAQSHGT 249
QUERY: 69 LTVLTPDQLNS 79
+||| ++ |
20 SBJCT: 250 VTVLDLNRYKS 260

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus Musculus* Follistatin-like Protein shown in Table 1D.

25 Table 1D. BLASTP of FCTR1 against *Mus Musculus* Follistatin-like Protein (SEQ ID NO:39)

PTNR:SPTREMBL-ACC:Q61581 FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) - MUS MUSCULUS (MOUSE), 238 AA.
LENGTH = 238

SCORE = 149 (52.5 BITS), EXPECT = 1.5×10^{-10} , P = 1.5×10^{-10}
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

35 QUERY: 15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
|||| +++++| |||++ |||||+ + + | | | | | + | | | | +||+
SBJCT: 165 LPGDRENLAIQTRGGPEKHEVTGWLVSPLSKEDAGEYECHASNSQGQASAAKITVV 222

40 The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* MAC25 protein shown in Table 1E.

45 Table 1E. BLASTP of FCTR1 against *Homo sapiens* MAC25 protein (SEQ ID NO:40)

PTNR:SPTREMBL-ACC:Q07822 MAC25 PROTEIN - HOMO SAPIENS (HUMAN), 277 AA.
LENGTH = 277

50 SCORE = 149 (52.5 BITS), EXPECT = 3.2×10^{-10} , P = 3.2×10^{-10}
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFEVTGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
|||| +++++| |||++ |||||+ + + | | | | | + | | | | +||+
SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWLVSPLSKEDAGEYECHASNSQGQASASAKITVV 266

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus musculus* MAC25 protein shown in Table 1F.

Table 1F. BLASTP of FCTR1 against *Mus musculus* MAC25 protein (SEQ ID NO:41)

PTNR:SPTREMBL-ACC:O88812 MAC25 - MUS MUSCULUS (MOUSE), 281 AA
 LENGTH = 281
 SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)
 QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
 |||| ++++| ||||++ |||||+ + + | | | | | + | | | + || +
 SBJCT: 208 LPGDRENLAIQTRGGPEKHEVTGWLVSPLSKEDAGEYECHASNSQQQASAAKITVV 265

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* Prostacyclin-stimulating factor shown in Table 1G.

Table 1G. BLASTP of FCTR1 against *Homo sapiens* Prostacyclin-stimulating factor (SEQ ID NO:42)

PTNR:SPTREMBL-ACC:Q16270 PROSTACYCLIN-STIMULATING FACTOR - HOMO SAPIENS (HUMAN), 282 AA
 LENGTH = 282
 SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
 IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)
 QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
 |||| ++++| ||||++ |||||+ + + | | | | | + | | | + || +
 SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWLVSPLSKEDAGEYECHASNSQQQASASAKITVV 266

The amino acid sequence of FCTR1 also had 18/44 bases (40%) identical, and 25/44 bases (56%) positive for rat Colorectal cancer suppressor shown in Table 1H.

Table 1H. BLASTP of FCTR1 against rat Colorectal cancer suppressor (SEQ ID NO:43)

PTNR:PIR-ID:B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS)
 LENGTH = 144
 SCORE = 78 (27.5 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
 IDENTITIES = 18/44 (40%), POSITIVES = 25/44 (56%)
 QUERY: 33 FEVTGW--LQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTP 74
 |++ | | + | | |||| | + | + | | | ++ | | | |
 SBJCT: 101 FQIVGGSNLRILGVVKSDEGFYQCVANEAGNAQSSAQLIVPKP 144
 SCORE = 37 (13.0 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
 IDENTITIES = 8/19 (42%), POSITIVES = 12/19 (63%)
 QUERY: 1 MASIEWRKDGLDIQL-PGD 18
 | + | | + | + | + |||
 SBJCT: 30 MPTIHWQKNQQLTPNPGD 48

The amino acid sequence of FCCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive to bases 55-137, and 24/68 bases (35%) identical, and 37/68 bases (54%) positive to bases 166-225 of *Homo sapiens* PTPsigma-(Brain) Precursor shown in Table 1I.

Table 1I. BLASTP of FCCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:44)

PTNR:TREMBLNEW-ACC:AAD09360 PTPSIGMA-(BRAIN) PRECURSOR - HOMO SAPIENS (HUMAN), 1502 AA.

LENGTH = 1502

SCORE = 109 (38.4 BITS), EXPECT = 0.00010, P = 0.00010
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY: 14 QLPGDD-PHISVQFRG---GPQRFVETGW-----LQIQAVR-PSDEGTYRCLARNALG 61
| | | ++ + | | | + | + | + | | | + | + | + |
SBJCT: 55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLR IQPLRTPRDENVYECVAQNSVG 114

QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85
++ | | | | | | | +
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 77 (27.1 BITS), EXPECT = 0.25, P = 0.22
IDENTITIES = 24/68 (35%), POSITIVES = 37/68 (54%)

QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALG-Q 62
| | | | + | | | + + + | | | + + + | + | + | + | +
SBJCT: 166 ITWFKDFLPV-----DPSAS---NGRIKQLR-SGALQIESSEETDQGYECVATNSAGVR 216

QUERY: 63 VEAPASLTV 71
+ | + | |
SBJCT: 217 YSSPANLYV 225

The amino acid sequence of FCCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive for amino acids 55-137 and 26/69 bases (37%) identical, and 38/69 (54%) positive for amino acids 166-234 of *Homo sapiens* Protein-Tyrosine Phosphatase Sigma shown in Table 1J.

Table 1J. BLASTP of FCCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:45)

PTNR:SPTREMBL-ACC:Q13332 PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, S PRECURSOR (EC 3.1.3.48) (PROTEIN-TYROSINE PHOSPHATASE SIGMA) (R-PTP-SIGMA) (PTPRS) - HOMO SAPIENS (HUMAN), 1948 AA.
LENGTH = 1948

SCORE = 109 (38.4 BITS), EXPECT = 0.00013, P = 0.00013
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY: 14 QLPGDD-PHISVQFRG---GPQRFVETGW-----LQIQAVR-PSDEGTYRCLARNALG 61
| | | ++ + | | | + | + | + | | | + | + | + |
SBJCT: 55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLR IQPLRTPRDENVYECVAQNSVG 114

QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85
++ | | | | | | | +
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 88 (31.0 BITS), EXPECT = 0.023, P = 0.022
IDENTITIES = 26/69 (37%), POSITIVES = 38/69 (55%)

QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFEV---GWLQIQAVRPSDEGTYRCLARNAL 60
 | | | | | + | | | + | | | | | + | | | + | | | +
 SBJCT: 166 ITWFKDFLE SASNGRIK-QLRS--ETFESTPIRGALQIESSE QGKYECVATNSA 222
 5 QUERY: 61 G-QVEAPASLTV 71
 | + + | | |
 SBJCT: 223 GVRYSSPANLYV 234

A ClustalW analysis comparing the protein of the invention with related protein
 sequences is given in Table 1K, with FCTR1 shown on line 2. In the ClustalW alignment of the
 FCTR1 protein, as well as all other ClustalW analyses herein, the black outlined amino acid
 residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve
 structural or functional properties), whereas non-highlighted amino acid residues are less
 conserved and can potentially be mutated to a much broader extent without altering protein
 structure or function.

Table 1K. ClustalW Analysis of FCTR1

- 1) Q07822 MAC25 PROTEIN. (SEQ ID NO:40)
- 2) Q16270 PROSTACYCLIN-STIMULATING FACTOR. (SEQ ID NO:42)
- 3) Q61581_FOLLISTATIN-LIKE 2: FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) (SEQ ID NO:39)
- 4) BAA21725 IGFBP-LIKE PROTEIN (SEQ ID NO:38)
- 5) FCTR1 (SEQ ID NO:2)
- 6) B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS) (SEQ ID NO:43)

20 25 30 35 40 45 50 55 60	Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098 Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098 Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098 Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098 Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098 Q07822 Q16270 Q61581_ BAA21725 FCTR1 B40098	MERASLRALLFGPAGLLLLLLPLSSSSSSDTCGPCEPASCPPLPPLGCLLGETRDACGCC MERPSLRALLLGAAGLLLLLLPLSSSSSSDTCGPCEPASCPPLPPLGCLLGETRDACGCC MERP PRALLLGAAGLLLLLLPLSSSSSSDACGR MPRLPLLLLLLPLSLARGLGLRDAG RRHPECSPCQDRCPPAPSPCPAPWISARDECGCC PMCARGEGEPCGGGAGRGYCAPGMECVKSRKRRKGKAGAAAGGPVSGVCVCKSRYPVC PMCARGEGEPCGGGAGRGYCAPGMECVKSRKRRKGKAGAAAGGPVSGVCVCKSRYPVC ARCLGAEAGASCG GPVGSRCGPGLVCA SR ASGTAPEG T GLCVCAQRGAVC GSDGTTPSGCQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVGTGAQV GSDGTTPSGCQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVGTGAQV GSNGITTPSGCQLRAASLRAESRGEKP ITQVSKGTCEQGPSIVTPPKDIWNVGTGAQV GSDGRSYSSICALRLRLRARHAPRAHHG LHKARDGPEFAFVVMPPRD IHNVTCIQV AFMGDTIVLLKCEVI G DPMPTIHWQKNQDLTPNPGDSRVVVPWFENHESNLVAYESMDI YLSCEVIGIPTPVLIWNKVKRGHYGVORTELLPGDRNLAIQTRGGPEKHEVTGWVLMSP YLSCEVIGIPTPVLIWNKVKRGHYGVORTELLPGDRNLAIQTRGGPEKHEVTGWVLMSP YLSCEVIGIPTPVLIWNKVKRHSGVORTELLPGDRNLAIQTRGGPEKHEVTGWVLMSP YLSCEVKAVPTPVLTWKKVKHSPEGTEGLEELPGDHVNIAVQVRGGPSDHEITTSWILLNP MASIEWRKDGLDIO.....LPGDDPHISVQFRGGPQRFEV---GWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQLRSLNLVPEEEAESEEND EFEGAVSGKPVPTVNMKNGDVVV.....ISDYFOIVGGSN.....LRILG LSKEDAGEYECHASNSQGQASASAKITVVDALHEIAS.....EKRR.... LSKEDAGEYECHASNSQGQASASAKITVVDALHEIPV.....KKGEGAE LSKEDAGEYECHASNSQGQASAAAKITVVDALHEIPL.....KKGEGAQ LRKEDEGVYHCHAANAICEAQSHTVTVLEDLNRYKSE.....YSSVPCD VRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIPQLRSLNLVPEEEAESEEND VVKSDEGFYQCVAEENEAGNAQSSAQLTVPKP.....
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Q07822
Q16270
Q61581_
BAA21725
FCTR1

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YY

IGFBP is expressed in neurostem cell and developing central nervous system. MAC-25, a follistatin like protein is a growth suppressor of osteosarcoma cells, and meningiomas. DCC is expressed in most normal tissues especially in colonic mucosa, but is deleted in colorectal cancers.

Since FCTR1 has similarity to these proteins (shown in BlastP, Tables 1C-1J, and in clustalW, Table 1K) it is likely that it has similar function. Therefore FCTR1 could function as on or more of the following: a tumor suppressor gene or regulator of neurological system development.

Based on the protein similarity and tissue expression, FCTR1 may be useful in the following diseases and uses:

- (i) Tissue regeneration in vitro and in vivo
- (ii) Neurological disorders, neurodegenerative disorders, nerve trauma
- (iii) Reproductive health
- (iv) Immunological disorders, allergy and infection
- (v) In cancer as a diagnostic and prognostic marker, as well as a protein therapeutic

FCTR2

FCTR2 (alternatively referred to herein as AC012614_1.0.123), is a growth factor bearing sequence similarity to human KIAA1061 protein and to genes involved in neuronal development and reproductive physiology (e.g., cell adhesion molecules, follistatin, roundabout and frazzled). FCTR2 is a full-length clone of 5502 nucleotides, including the entire coding sequence of a 815 amino acid protein. This sequence is expressed in glioma, osteoblast, other cancer cells, lung carcinoma, small intestine (This sequence maps to Unigene Hs.123420 which is expressed in brain, breast, kidney, pancreas, pooled tissue).

A FCTR2 ORF begins with an ATG initiation codon at nucleotides 420-422 and ends with a TGA codon at nucleotides 2865-2867. Putative untranslated regions upstream from the initiation codon and downstream from the termination codon are underlined in Table 2A, and the start and stop codons are in bold letters.

Table 2A. FCTR2 Nucleotide Sequence (SEQ ID NO:3).

CAATTTACACAGGAAACAGCTATGCCATGATTACGCAAGTTGGTACCGAGCTCGGATCCACTAGTAACGGCCGCCAGTG
TGCTGGAATTCGGCTTACTCACTATAGGGCTCGAGCGGCTGCCCGGGCAGGTCATTAAATCCATTTCCTTTAGAGTATC
ACAGCTTTCTCCTTCACTGACCACCCCTTGCTTCCTGTGAGAAAGCCCTGGACAGAACTCTCTGTGGGATCTGCCCATG

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SBJCT: 1381 GGT TTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 1440
QUERY: 2224 TGATGCCCCGACCATCGGCCTGCACCACCATGGCTGCGTGCCGATGGCAC 2283
|||||
SBJCT: 1441 TGATGCCCCCAAGACCATCGGCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 1500
QUERY: 2284 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCTCTGCTG 2343
|||||
SBJCT: 1501 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCTCTGCTG 1560
QUERY: 2344 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 2403
|||||
SBJCT: 1561 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 1620
QUERY: 2404 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 2463
|||||
SBJCT: 1621 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 1680
QUERY: 2464 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 2523
|||||
SBJCT: 1681 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 1740
QUERY: 2524 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 2583
|||||
SBJCT: 1741 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 1800
QUERY: 2584 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTTGAGCTGTCCACGG 2643
|||||
SBJCT: 1801 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTTGAGCTGTCCACGG 1860
QUERY: 2644 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTNNN 2703
|||||
SBJCT: 1861 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTGGG 1920
QUERY: 2704 NNNNTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 2763
|||||
SBJCT: 1921 GGGGTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 1980
QUERY: 2764 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCTAG 2823
|||||
SBJCT: 1981 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCTAG 2040
QUERY: 2824 GTATAAANNNNNNNACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCAGAG 2883
|||||
SBJCT: 2041 GTATAAAGGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCAGAG 2100
QUERY: 2884 CCCTGGGCCAAGGAACACCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2943
|||||
SBJCT: 2101 CCCTGGGCCAAGGAACACCCCTAGTCCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2160
QUERY: 2944 ATTTTTCAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 3003
|||||
SBJCT: 2161 ATTTTTCAGACAAAAGCAAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCCTTG 2220
QUERY: 3004 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 3063
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SBJCT: 2221 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 2280
QUERY: 3064 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 3123
|||||
SBJCT: 2281 ATGATTTATGCCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTTCTG 2340
QUERY: 3124 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 3183
|||||
SBJCT: 2341 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 2400
QUERY: 3184 AGCAGACACCTCTGTCTAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 3243
|||||
SBJCT: 2401 AGCAGACACCTCTGTCTAGTTGCCTTCACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 2460

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QUERY: 3244 AGACTTTGCCCTGACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGAGCAGGGGCTCCCT 3303
|||
SBJCT: 2461 AGACTTTGCACGGAGTGGCCCGGAAGCAGAGGCCGACCAGGAGGGGCTCCCT 2520

5 QUERY: 3304 CCCGAAGTCAAAGCCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 3363
|||
SBJCT: 2521 CCCGAAGTCAAAGCCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 2580

10 QUERY: 3364 CTTGCTTTTCTTTCCATTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 3423
|||
SBJCT: 2581 CTTGCTTTTCTTTCCATTGACTTGCTGTAAGCCTGAGGGAGAGCCAACAAGACTTACTG 2640

15 QUERY: 3424 CATCTGGGGGATGGGGAAATCACTCACTTTATTTTGAAATTTTGATTNNNNNNNNNT 3483
|||
SBJCT: 2641 CATCTGGGGGATGGGGAAATCACTCACTTTATTTTGAAATTTTGATTAAAAAAAAT 2700

20 QUERY: 3484 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACATATATCCTTC 3543
|||
SBJCT: 2701 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAACATATATCCTTC 2760

25 QUERY: 3544 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCACATCCCACAGCCAGAAAGAAC 3603
|||
SBJCT: 2761 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCACAACCCACATCCCACAGCCAGAAAGAAC 2820

30 QUERY: 3604 AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 3663
|||
SBJCT: 2821 AATGGTCATCTGAGAATACTGGCCCTGTCGACTATTGCCACCCTGCTTCTCCAAGAGCAG 2880

35 QUERY: 3664 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCAAAAAACCAGAACA 3723
|||
SBJCT: 2881 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCAAAAAACCAGAACA 2940

40 QUERY: 3724 AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3783
|||
SBJCT: 2941 AGTTCTGTGTGCCTCCTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3000

45 QUERY: 3784 CCAGATTGAGGGCAGACTGGGCTTGCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3843
|||
SBJCT: 3001 CCAGATTGAGGGCAGACTGGGCTTGCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3060

50 QUERY: 3844 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAC 3903
|||
SBJCT: 3061 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAC 3120

55 QUERY: 3904 AGATTTTGTTTTCTACCTGTGGCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3963
|||
SBJCT: 3121 AGATTTTGTTTTCTACCTGTGGCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3180

60 QUERY: 3964 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAATAC 4023
|||
SBJCT: 3181 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTTCTTACCCACATTCCCCAATCAATAC 3240

65 QUERY: 4024 ACACACACTGCAGAAGCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 4083
|||
SBJCT: 3241 ACACACACTGCAGAAGCCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 3300

70 QUERY: 4084 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 4143
|||
SBJCT: 3301 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCCACATAGCCCT 3360

QUERY: 4144 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 4203
|||
SBJCT: 3361 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 3420

QUERY: 4204 TGAGTGGAACCTACATGTGTCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 4263
|||
SBJCT: 3421 TGAGTGGAACCTACATGTGTCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 3480

QUERY: 4264 AGAGGTGGTCTCACCACAGACGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 4323
|||

QUERY: 5344 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTACAACTGAT 5403
 SBJCT: 4561 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTACAACTGAT 4620
 5 QUERY: 5404 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAGAATCATCAAGAAAGCTATTTATA 5463
 SBJCT: 4621 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAAGAATCATCAAGAAAGCTATTTATA 4680
 10 QUERY: 5464 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 5502
 SBJCT: 4681 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 4719

The FCTR2 amino acid sequence has 473 of 810 amino acid residues (58%) identical to,
 and 616 of 810 residues (76%) positive with, the 850 amino acid residue proteins from *Homo*
 15 *sapiens* KIAA1263 Protein fragment (ptnr: TREMBLNEW-ACC:BAA86577) (SEQ ID NO:47)
 (Table 2D).

**Table 2D. BLASTP of FCTR2 against *Homo sapiens* KIAA1263 Protein fragment (SEQ ID
 NO:47)**

ptnr:TREMBLNEW-ACC:BAA86577 KIAA1263 PROTEIN - Homo sapiens (Human), 850 aa
 (fragment)
 Length = 850
 Score = 2573 (905.7 bits), Expect = 2.0e-267, P = 2.0e-267
 Identities = 473/810 (58%), Positives = 616/810 (76%)
 20
 25
 30
 35
 40
 45
 50
 55
 60
 QUERY: 10 LFRLSLKRALSSCPDLFGLSSRNELLASCGKKFCSRGRSVCVLSRKTGEPECQCLEACRPS 69
 | | | | | + | ++ | | | | | + | | | | + | | ++ | +
 SBJCT: 40 LMRLRHKEKNQESSRVKGFMIQDGPFGSCENKYCGLGRHCVTSRETGQAECACMDLCKRH 99
 QUERY: 70 YVPVCGSDGRFYENHCKLHRAACLLGKRITVIHSDKDCFLKGDCTMAGYARLKNVLLALQ 129
 | | | | | | | | | | ++ | | | | ++ | ++ | ++ | | | | | + | + | + | | |
 SBJCT: 100 YKPVCSDGEFYENHCEVHRAACLLKKQKITIVHNEDCFKGDCKKTTEYSKMKNMLLDLQ 159
 QUERY: 130 TRLQPLQEGDSRQ-DPASQKRLLVESLFRDLADGNGHLSSSELAQHVLKKQDLDEDLLG 188
 + + | | ++ | | + | + | | + + | | | + | + | + | + | + |
 SBJCT: 160 NQKYIMQENENPNNGDDISRKLLVDQMFKYFDADSNGLVDINELTQ-VIKQEELGKDLFD 218
 QUERY: 189 CSPGDLRLRFDDYNSDSSLTLREFYMAFQVQVLSLAPEDRVSVTTVTVGLSTVLTCAVHGD 248
 | + | | + | + | + | | | | | | + | | | + + | | | | | | + |
 SBJCT: 219 CTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQKLSITAATVGQSAVLSCAIQGT 278
 QUERY: 249 LRPPIIWKRNGLTLNFDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVL 308
 | | | | | | | | + | | | | | | | + | | | | | + | + | + | + | + |
 SBJCT: 279 LRPPIIWKRNIIILNLDLEDINDFGDDGSLYITKVTTTHVGNYTCTYADGYEQVYQTHIF 338
 QUERY: 309 QVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANG 368
 | | | | | | | | | | + | | | | | | | | | | ++ | | | | + | + | + | + | |
 SBJCT: 339 QVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKQPLGWLKNGIDITPKLSKQLTLQANG 398
 QUERY: 369 SELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLSVGNMFY 428
 | + | | + | | | | | | | | | | | | | + | | | | | | | | + | | | |
 SBJCT: 399 SEVHISNVRYEDTGAYTCIAKNEAGVEDISSLFVEDSARKTLANILWREEGLGIGNMFY 458
 QUERY: 429 VFSDDGIIVIHPVDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNVRNRYIY 488
 | | + | | | | | + | | | | + | + | + | + | + | + | | | | | + | + | + |
 SBJCT: 459 VFYEDGIKVIQPIECEFORHIKPKSEKLLGFQDEVCPKAEGDEVQRCVWASAVNVKDKFIY 518
 QUERY: 489 VAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRLSLQVIT 548
 | | | | | | + | + | + | + | + | + | | | | | | | | + | + | + | | |
 SBJCT: 519 VAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHDQVWVLSWGTLEKTSPTLQVIT 578
 QUERY: 549 EASTGQSQHLIRT-----PFAGVDDFFIPPTNLIINHIFGFIFNKSDPAVHKVDLETMM 603


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SUBJECT: 579 LASGNVPHTT PVGKQFDRVDDFFIPTTLIITHMRFGFILHKL QKIDLETMS 638

QUERY: 604 PLKTIGLHHHCVPQAMAHTHLGGYFFIQCRQDSPASAAARQLLVDSVTDSVLGPNGDVTG 663
      + ||| | + |||++|+|||||+|| + || + + |++| |||||+| ||||
SUBJECT: 639 YIKTNLKDYKCVPQSLAYTHLGGYYFIGCKPDSTGAVSPQVMVDGVTDSDVIGFNSDVTG 698

QUERY: 664 TPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQYN 723
      ||+ |||| ++|| + || |+||||| ++ + || ||||| |||||++|||
SUBJECT: 699 TPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIYTNLHISDLAQPSFTEAHQYN 758

QUERY: 724 IYAALHTEPDDLFLLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPAR 783
      || + |+ |+|+|+|+||| |+|+||| || +| ++| ||||| |||+|++
SUBJECT: 759 IYGSSSTQTDVLFVELSSGKVMIKS LKEPLKAEEWPWRNKRNRQIQDSGLFGQYLMTPSK 818

QUERY: 784 ESLFLINGRQNTLRCEVSGIKGTTVVWVGE 814
      +|||+++|| | ||++ ++ | ||+|||+
SUBJECT: 819 DSLFILDGRLNKLNCEITEVEKGNTVIWVG D 849

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Amino acids 123-815 of FCTR2 also have 693 of 693 amino acid residues (100%) identical to, the 693 amino acid residue protein fragment of KIAA1061 Protein from *Homo sapiens* (ptnr: TREMBLNEW-ACC: BAA83013) (SEQ ID NO:48) (Table 2E).

Table 2E. BLASTP of FCTR2 against KIAA1061 Protein [Fragment] (SEQ ID NO:48)

ptnr:TREMBLNEW-ACC:BAA83013 KIAA1061 PROTEIN - Homo sapiens (Human),
693 aa (fragment).

Length = 693

Score = 3623 (1275.4 bits), Expect = 0.0, P = 0.0
Identities = 693/693 (100%), Positives = 693/693 (100%)

QUERY: 123 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNGHLSSSELAQHVLKKQDL 182

SBJCT: 1 NVLLALQTRLOPLQEGDSRQDPASQKRLLVESLFRDLADGNGHLSSSELAQHVLKKQDL 60

QUERY: 183 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 242

SBJCT: 61 DEDLLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTVTVGLSTVLT 120

QUERY: 243 CAVHGDLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302

SBJCT: 121 CAVHGDLRPPIIWKRNGLTNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 180

QUERY: 303 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 362

SBJCT: 181 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 240

QUERY: 363 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDEDISSLFIEDSARKTLANILWREEGLS 422

SBJCT: 241 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLS 300

QUERY: 423 VGNMFYVFSDDGIIVIHVPDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 482

SBJCT: 301 VGNMFYVFSDDGIIVIHVPDCEIQRHLKPTEKIFMSYEEICPQREKNATQPCQWVSAVNV 360

QUERY: 483 RNRYIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 542

SBJCT: 361 RNRYYVAQPALSRVLVVDIQAKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 420

QUERY: 543 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIRFGFIFNKSDPAVHKVDLETM 602

SBJCT: 421 SLOVITEASTGOSOH LIRTPFAGVDDFFIPPTNLI INHIRFGFI FNKSDPAVHKVDLETM 480

QUERY: 603 MPLKTIGLHHH●●●PQAMATHLGGYFFIQCRQDSPASAAARQLLVDS●●●SVLGPNGDVT 662
 SBJCT: 481 MPLKTIGLHHHGCVPQAMATHLGGYFFIQCRQDSPASAAARQLLVDSVTDSVLGPNGDVT 540
 QUERY: 663 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 722
 SBJCT: 541 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 600
 QUERY: 723 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 782
 SBJCT: 601 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 660
 QUERY: 783 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 815
 SBJCT: 661 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 693

The amino acid sequence of the FCTR2 protein has 451 of 772 amino acid residues
 (58%) identical to, and 586 of 772 residues (75%) positive with, the 773 amino acid residue
 proteins hypothetical protein DKFZp566D234.1 from *Homo sapiens* (fragments) (ptnr:
 SPTREMBL-ACC: CAB70877.1) (SEQ ID NO:49) (Table 2F).

**Table 2F. BLASTP of FCTR2 against hypothetical protein DKFZp566D234.1 (SEQ ID
 NO:49)**

>GI|11360192|PIR||T46283 HYPOTHETICAL PROTEIN DKFZP566D234.1 - HUMAN (FRAGMENTS)
 GI|6808053|EMBL|CAB70877.1| (AL137695) HYPOTHETICAL PROTEIN [HOMO SAPIENS]
 LENGTH = 773
 SCORE = 911 BITS (2354), EXPECT = 0.0
 IDENTITIES = 451/772 (58%), POSITIVES = 586/772 (75%), GAPS = 7/772 (0%)
 QUERY: 49 CVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLKGKRTVIHSDKDCFL 108
 SBJCT: 2 CVTSRETGQAECACMDLCKRHYKPVCGSDGEFYENHCEVHRAACLKKQKITIVHNEDCF 61
 QUERY: 109 KGDTCTMAGYARLKNVLLALQTRLQPLQEGDSRQ-DPASQKRLLVESLFRDLADAGNGHL 167
 SBJCT: 62 KGDKCKTTECSKMKNMLLDLQNRQYIMQENENPNGDDISRKKLLVDQMFKYFDADSNDLV 121
 QUERY: 168 SSSELAQHVLKKQDLDEDLGCSPGDLLRFDDYNSDSSLTLREFYMAFQVVQLSLAPEDR 227
 SBJCT: 122 DINELTQ-VIKQEELGKDLFDCTLYVLLKYDDFNADKHLALEEFYRAFQVIQLSLPEDQK 180
 QUERY: 228 XXXXXXXXXXXXXXXCAVHGDRLRPPIIWKRNGLTLNFLDLEDINDFGEDDSLYITKVTTI 287
 SBJCT: 181 LSITAATVGQSAVLSCAIQGTLRPPIIWKRNIIILNGLLEDINDFGDDGSLYITKVTTT 240
 QUERY: 288 HMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW 347
 SBJCT: 241 HVGNYTCYADGYEQVYQTHIFQVNVPPVIRVYPESQAREPGVTASLRCHAEGIPKPQLGW 300
 QUERY: 348 LKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSA 407
 SBJCT: 301 LKNGIDITPKLSKQLTLQANGSEVHISNVRYEDTGAYTCIAKNEAGVEDISSLFVEDSA 360
 QUERY: 408 RKTLANILWREGLSVGNMFYVFSDDGIIVHPVDCEIQRHLKPTEKIFMSYEEICPQRE 467
 SBJCT: 361 RKTLANILWREGLGIGNMFYVFYEDGKIVIQPIECEFORHIKPKSEKLLGFQDEVCPIAE 420
 QUERY: 468 KNATQPCQWVSAVNVNRNRIYVAQPALSRVLVVDIQAQKVLQSIGVDPLPAKLSYDKSHD 527
 SBJCT: 421 GDEVQRCVWASAVNVKDKFIYVAQPTLDRVLIVDVQSQKVVQAVSTDPVPVKLHYDKSHD 480

QUERY: 528 QVWVLSWGDVHKSRPSLQVITEASTGQSQHLIRT-----PFAGVDDFFIPPTNLIINHIR 582
 SBJCT: 481 QVWVLSWGTLPPTLQVITLASGNVPHHTIHTQPVGKQFDRVDDPTTLIITHMR 540
 5 QUERY: 583 FGFIFNKSDPAVHKVDLETMMPLKTIGLHHHCVPQAMAHTHLGGYFFIQCQRQDSPASAA 642
 SBJCT: 541 FGFILHKDEAALQKIDLETMSYIKTINLKDYKCVQPSLAYTHLGGYFFIGCKPDSTGAVS 600
 10 QUERY: 643 RQLLVDSVTDVSLGPNGDVTGTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQ 702
 SBJCT: 601 PQVMVDGVTDSVIGFNSDVTGTPYVSPDGHYLVSINDVKGLVRVQYITIRGEIQEAFDIY 660
 15 QUERY: 703 INSGISDLAFQRSFTESNQYNIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWG 762
 SBJCT: 661 TNLHISDLAFQPSFTEAHQYNIYGSSSTQTDVLFVELSSGKVKMIKSLKEPLKAEWPNW 720
 20 QUERY: 763 GTHRIMRDSGLFGQYLLTPARESFLINGRQNTLRCEVSGIKGGTTVVWVGE 814
 SBJCT: 721 RKNRQIQDSGLFGQYLMTPSKDSLFIIDGRLNKLNCEITEVEKGNTVIWVGD 772

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 90 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastin-Related Protein 1 Precursor from *Rattus Norvegicus* (ptnr: GenBank Acc:Q62632) (SEQ ID NO:50) (Table 2G).

Table 2G. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Rattus Norvegicus* (SEQ ID NO:50)

>GI|2498392|SP|Q62632|FRP_RAT FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
 GI|1083669|PIR||S51361 FOLLISTATIN-RELATED PROTEIN PRECURSOR - RAT
 GI|536900|GB|AAA66063.1| (U06864) FOLLISTATIN-RELATED PROTEIN PRECURSOR [RATTUS NORVEGICUS]
 LENGTH = 306
 SCORE = 86.4 BITS (213), EXPECT = 1E-15
 IDENTITIES = 61/194 (31%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)
 35 QUERY: 38 CGKKFCSRGRSVCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
 SBJCT: 29 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLGTGSK 87
 40 QUERY: 98 ITVIHSDKCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
 SBJCT: 88 IQVDYDGHCKEKKSVSPSPVVCYQANRDELRRRIIQWLEAEIIP----DGWFSKGSNY 143
 45 QUERY: 149 RLLVESLFRDLADGNHGLSSSELAQHVLK-----KQDLDEDLLGCSPGDLLRF 197
 SBJCT: 144 SEILDYKFKSFD-NGDSHLDSSEFLKFVEQNETAVNITAYPNQENNKLLRGLCVDALIEL 202
 50 QUERY: 198 DDYNSDSSLTLREF 211
 SBJCT: 203 SDENADWKLSFQEF 216

The amino acid sequence of the FCTR2 protein has 61 of 194 amino acid residues (31%) identical to, and 89 of 194 residues (45%) positive with, the 306 amino acid residue protein Follastin-Related Protein 1 Precursor from *Mus musculus* (GenBank Acc:Q62356) (SEQ ID NO:51) (Table 2H).

Table 2H. BLASTP of FCTR2 against Follastatin-Related Protein 1 Precursor from *Mus musculus* (SEQ ID NO:51)

>GI|6679871|REF|NP_032073.1| FOLLISTATIN-LIKE [MUS MUSCULUS]
 GI|2498391|SP|Q62356|FRP_MOUSE FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR (TGF-BETA-INDUCIBLE PROTEIN TSC-36)
 GI|481186|PIR|S38251 FOLLISTATIN-RELATED PROTEIN - MOUSE
 GI|349006|GB|AAC37633.1| (M91380) TGF-BETA-INDUCIBLE PROTEIN [MUS MUSCULUS]
 LENGTH = 306

SCORE = 85.2 BITS (210), EXPECT = 3E-15
 IDENTITIES = 61/194 (31%), POSITIVES = 89/194 (45%), GAPS = 26/194 (13%)

QUERY: 38 CGKKFCSRGSRVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
 | | | | ++ | || | | + | | | | + | | | + | | | | +
 SBJCT: 29 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 87

QUERY: 98 ITVIHSDKDCFLKGD-----CTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
 | | + | | | | | + | + | + + | | | |
 SBJCT: 88 IQVDYDGHCKEKKSSASPSASPVVCYQANRDELRRRLIQWLEAEIIP----DGWFSKGSNY 143

QUERY: 149 RLLVESLFRDLADGNHGLSSSELAQHVLKK-----QDLDEDLLGCSPGDLLRF 197
 +++ | + | + | + | | | + | + | + ++ | | +
 SBJCT: 144 SEILDYFKSFD-NGDSDLDSSEFLKFVEQNETAINITYADQENNKLLRSLCVDALIEL 202

QUERY: 198 DDYNSDSSLTLREF 211
 | | + | + + | |
 SBJCT: 203 SDENADWKLSPQEF 216

The amino acid sequence of the FCTR2 protein has 63 of 193 amino acid residues (32%) identical to, and 89 of 193 residues (45%) positive with, the 299 amino acid residue protein Follastatin-Related Protein from the African Clawed Frog (GenBank Acc:JG0187) (SEQ ID NO:52) (Table 2I).

Table 2I. BLASTP of FCTR2 against Follastatin-Related Protein from the African Clawed Frog (SEQ ID NO:52)

>GI|7512162|PIR|JG0187 FOLLISTATIN-RELATED PROTEIN - AFRICAN CLAWED FROG
 LENGTH = 299

SCORE = 81.8 BITS (201), EXPECT = 3E-14
 IDENTITIES = 63/193 (32%), POSITIVES = 89/193 (45%), GAPS = 25/193 (12%)

QUERY: 38 CGKKFCSRGSRVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
 | | | | ++ | | + | | | + | | | + | | | + |
 SBJCT: 28 CANVFCGAGRECAVTEK-GDPTCDCIECKSHKRPVCGSNGKTYLNHCELHRDACLTGSK 86

QUERY: 98 ITVIHSDKDCFLK-GDT-----CTMAGYARL-KNVLLALQTRLQPLQEGDSRQDPASQK 148
 | | + | | | | | + + + | + | | + | | | + |
 SBJCT: 87 IQVDYDGHCKEKTSDTPAAVPVACYQSDRDEMRRRVIHWLQTEITP----DGWFSKGSNDY 142

QUERY: 149 RLLVESLFRDLADGNHGLSSSELAQHVLKKQDL-----DED----LLGCSPGDLLRFD 198
 +++ | + | | + | | + | + + | | + | | +
 SBJCT: 143 SEILDYFKKFD-DGDSHLDSEFLQSFLEQSQSTNITYKDEETNRMLKSLCVEALIELS 201

QUERY: 199 DYNSSDSSLTLREF 211
 | | + | | | |
 SBJCT: 202 DENADWKLKNEF 214

The amino acid sequence of the FCTR2 protein has 59 of 194 amino acid residues (30%) identical to, and 90 of 194 residues (45%) positive with, the 308 amino acid residue protein Follistatin-Related Protein 1 Precursor from *Homo sapiens* (GenBank Acc:Q12841) (SEQ ID NO:53) (Table 2J).

Table 2J. BLASTP of FCTR2 against Follistatin-Related Protein 1 Precursor from *Homo sapiens* (SEQ ID NO:53)

```
>GI|5901956|REF|NP_009016.1| FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
GI|2498390|SP|Q12841|FRP_HUMAN FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
GI|1082372|PIR|S51362 FOLLISTATIN-RELATED PROTEIN - HUMAN
GI|536898|GB|AAA66062.1| (U06863) FOLLISTATIN-RELATED PROTEIN PRECURSOR [HOMO
SAPIENS]
GI|3184393|DBJ|BAA28707.1| (D89937) FOLLISTATIN-RELATED PROTEIN (FRP) [HOMO SAPIENS]
GI|12652619|GB|AAH00055.1|AAH00055 (BC000055) FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
LENGTH = 308

SCORE = 82.9 BITS (204), EXPECT = 1E-14
IDENTITIES = 59/194 (30%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

QUERY: 38 CGKKFCSRGRSVCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
          ||| | | ++ | ||| | |+| |+| |||||+|+ | |||+||| ||| | +
SBJCT: 31 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTGSK 89

QUERY: 98 ITVIHSDCKFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
          || + | | | | + | + ++ | + + | | | | |
SBJCT: 90 IQVDYDGHCKEKKSVSPSASPVCYQSNRDELRRRIIQWLEAEIIP----DGWFSKGSNY 145

QUERY: 149 RLLVESLFRDLADGNHGLSSSELAQHVLKK-----QDLDEDLLGCSPGDLLRF 197
          +++ |++ | ++ | ||| | + | + | + ++ | | | +
SBJCT: 146 SEILDKYFKNFD-NGDSRLDSSEFLKFVEQNETAINITYPDQENKLLRGLCVDALIEL 204

QUERY: 198 DDYNSDSSLTLREF 211
          | | | | + + ||
SBJCT: 205 SDENADWKLSTFQEF 218
```

The amino acid sequence of the FCTR2 protein has 35 of 69 amino acid residues (50%) identical to, and 45 of 69 residues (64%) positive with, the 315 amino acid residue Flik protein [*Gallus gallus*] (EMBL Acc:CAB42968.1) (SEQ ID NO:54) (Table 2K).

Table 2K. BLASTP of FCTR2 against Flik protein [*Gallus gallus*] (SEQ ID NO:54)

```
>GI|4837645|EMBL|CAB42968.1| (AJ238977) FLIK PROTEIN [GALLUS GALLUS]
LENGTH = 315

SCORE = 79.8 BITS (196), EXPECT = 1E-13
IDENTITIES = 35/69 (50%), POSITIVES = 45/69 (64%), GAPS = 1/69 (1%)

QUERY: 38 CGKKFCSRGRSVCVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
          ||| |||+ | ++ | ||| | |+| |+| |||||+|+ | |||+||| ||| | +
SBJCT: 31 CANVFCGRGAECAVTEK-GEPTCLCIEQCKPHGRPVCGSNGKTYLNHCELHRDACLTGSK 89

QUERY: 98 ITVIHSDCK 106
          || + |
SBJCT: 90 IQVDYDGH 98
```

The amino acid sequence of the FCTR2 protein has 49 of 152 amino acid residues (32%) identical to, and 65 of 152 residues (42%) positive with a 272-420 amino acid fragment and, 31

of 83 residues (37%) identical to and 44 of 83 residues (52%) positive with a 248-329 amino acid fragment, both of the 1375 amino acid residue Frazzled gene protein [*Drosophila melanogaster*] (GenBankAcc:T13822) (SEQ ID NO:55) (Table 2L).

Table 2L. BLASTP of FCTR2 against Frazzled gene protein [*Drosophila melanogaster*] (SEQ ID NO:55)

>GI|7511861|PIR|T13822 FRAZZLED GENE PROTEIN - FRUIT FLY (DROSOPHILA MELANOGASTER)
GI|1621115|GB|AAC47314.1| (U71001) FRAZZLED [DROSOPHILA MELANOGASTER]
LENGTH = 1375

SCORE = 69.4 BITS (169), EXPECT = 2E-10
IDENTITIES = 49/152 (32%), POSITIVES = 65/152 (42%), GAPS = 4/152 (2%)

QUERY: 243 CAVHGDLRPPPIIWKRNGLTNFLDLEDINDFGEDDSLVIKVTTHMGNVYCHASGH-EQ 301
| + | + | | | + | + | | + | | | | | +

SBJCT: 272 CVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGSLQISSAEDIDSGNYQCRASNTVDS 331

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQ 361
| + | | | | + | + | | | | | | | ++ |

SBJCT: 332 LDAQATVQVQEPKFIKAPKDTTAHEKDEPELKCDIWGKPKPVIRWLKNGDLITPNQDYM 391

QUERY: 362 LSLLANGSELHISSVRYEDTGAYTCIAKNEVG 393
| + | | | + | | + | + | |

SBJCT: 392 ---LVDGHNKILGLLNSDAGMFQCVGTNAAG 420

SCORE = 52.9 BITS (126), EXPECT = 1E-05
IDENTITIES = 31/83 (37%), POSITIVES = 44/83 (52%), GAPS = 2/83 (2%)

QUERY: 311 NVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVS-TQMSKQLSLLANGS 369
+ | | | | + | + | | | + | + | + | + | + | + |

SBJCT: 248 SVAPSFLVGPSPKTVREGDTVTLDVANGVPKPQIKWLRNGMDLDFNDLDSRFSIVGTGS 307

QUERY: 370 ELHISSVRYEDTGAYTCIAKNEV 392
| | | | + | | | | |

SBJCT: 308 -LQISSAEDIDSGNYQCRASNTV 329

The amino acid sequence of the FCTR2 protein has 53 of 177 amino acid residues (29%) identical to, and 78 of 177 residues (43%) positive with a 366-539 amino acid fragment, 51 of 170 residues (30%) identical to and 74 of 170 residues (43%) positive with a 276-438 amino acid fragment, 46 of 165 amino acid residues (27%) identical to, and 74 of 165 amino acid residues positive with a 185-341 amino acid fragment, 48 of 167 amino acid residues (28%) identical to and 70 of 167 amino acid residues (41%) positive with a 77-243 amino acid fragment, and 28 of 84 amino acid residues (33%) and 37 of 84 amino acid residues positive with a 56-139 amino acid fragment all of the protein 1395 residue Roundabout 1 protein [*Drosophila melanogaster*] (GenBankAcc:AAC38849.1) (SEQ ID NO:56) (Table 2M).

Table 2M. BLASTP of FCTR2 against Roundabout 1 protein [*Drosophila melanogaster*] (SEQ ID NO:56)

>GI|2804782|GB|AAC38849.1| (AF040989) ROUNDABOUT 1 [DROSOPHILA MELANOGASTER]
LENGTH = 1395

SCORE = 69.8 BITS (170), EXPECT = 1E-10
IDENTITIES = 53/177 (29%), POSITIVES = 78/177 (43%), GAPS = 11/177 (6%)

The amino acid sequence of the FCTR2 protein has 55 of 157 amino acid residues (35%) identical to, and 70 of 157 residues (47%) positive with a 626-775 amino acid fragment, 49 of 163 residues (30%) identical to and 71 of 163 residues (43%) positive with a 335-492 amino acid fragment, 32 of 85 amino acid residues (37%) identical to, and 48 of 85 amino acid residues (55%) positive with a 1305-1388 amino acid fragment, 37 of 143 amino acid residues (25%) identical to and 60 of 143 amino acid residues (41%) positive with a 183-319 amino acid fragment, 43 of 174 amino acid residues (24%) and 70 of 174 amino acid residues (39%) positive with a 711-884 amino acid fragment, and 46 of 165 residues (27%) identical to and 69 of 165 residues positive with a 831-884 amino acid fragment all of the protein 1395 residue Down Syndrome Cell Adhesion Molecule Precursor (CHD2) from *Homo Sapiens* (GenBankAcc:O60469) (SEQ ID NO:57) (Table 2N).

Table 2N. BLASTP of FCTR2 against Down Syndrome Cell Adhesion Molecule Precursor (SEQ ID NO:57)

>gi|12643619|sp|O60469|DSCA_HUMAN DOWN SYNDROME CELL ADHESION MOLECULE PRECURSOR (CHD2)
GI|6740013|GB|AAF27525.1|AF217525_1 (AF217525) DOWN SYNDROME CELL ADHESION MOLECULE [HOMO SAPIENS]
LENGTH = 2012

SCORE = 70.6 BITS (172), EXPECT = 6E-11
IDENTITIES = 55/157 (35%), POSITIVES = 75/157 (47%), GAPS = 7/157 (4%)

QUERY: 245 VHGDLRPPIIWKRNGLTNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQ 304
| || | | +++ | + | ++ | | | + ++ + | || | | | +
SBJCT: 620 VSGDLPITITWQKDGRIPIGSLGVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVE 679

QUERY: 305 THV-LQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-LKNGVDVST----QM 358
| | || | | | | | | | | | | + | | | | | +
SBJCT: 680 HQSQLIVRVPPKFFVQPRDQDIYGKAVILNCSAEGYPVPTIVWKFSGAGVPQFQPIAL 739

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVD 395
+ ++ +|+|| | | | ||+| | | |+|| |
SBJCT: 740 NGRIQVLSNGS-LLIKHVVEEDSGYYLCKVSNVDVGAD 775

SCORE = 50.6 BITS (120), EXPECT = 7E-05
IDENTITIES = 49/163 (30%), POSITIVES = 71/163 (43%), GAPS = 16/163 (9%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
|+| | + | || | || | ++ | + + | | | +
SBJCT: 335 CSVGTGEDQELSWYRNGEILNPGKNVRITGINHEN-LIMDHMVKSDGGAYQCFVRKDKLS 393

QUERY: 303 FQTH---VLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-----LKNGV 352
| + ||+ | + | + | | | + + | + | || | || |
SBJCT: 394 AQDYVQVLEDGTPKIIISAFSE-KVVSAPAEVSLMCNVKGTPLPTITWTLDLDDPILKGG- 451

QUERY: 353 DVSTQMSKQLSLLAN-GSELHISSVRYEDTGAYTCIAKNEGV 394
| ++|+ ++ | | |+|| + | | | | | |
SBJCT: 452 --SHRISQMITSEGNVVSYLNISSSQVRDGGVYRCTANNSAGV 492

SCORE = 47.9 BITS (113), EXPECT = 5E-04
IDENTITIES = 32/85 (37%), POSITIVES = 48/85 (55%), GAPS = 6/85 (7%)

QUERY: 333 LRCHAEGIPMPRITWLK--NGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKN 390
| | | | | + |+| | | + + |+ +||| + | |+ + ||+ | +|| | |
SBJCT: 1305 LPCKAVGDPSPAVKWMKDSNGTPSLVITDGRRSIFNGSFI-IRTVKAEDSGYYSCIANN 1363

QUERY: 391 EVGVDEDISSLFIE---DSARKTLA 412
| | | | + | | | ++
SBJCT: 1364 NWGSDEIIL QVPPDQPRLTVS 1388

SCORE = 42.9 BITS (100), EXPECT = 0.015
IDENTITIES = 37/143 (25%), POSITIVES = 60/143 (41%), GAPS = 6/143 (4%)

QUERY: 270 INDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGV 329
| | + | | | + | | | + | | | + + |
SBJCT: 183 IKDVQNE DGLYNRCITRHRYTGETRQNSARLFVSD--PANSAPSILDGFDHRKAMAGQ 240

QUERY: 330 AASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAK 389
| | | | | | | | + + + + + | | | + + | + | + |
SBJCT: 241 RVELPCKALGHPEPDYRWLKD--NMPLELSGRFQKTVTG--LLIENIRPSDSGSYVCEVS 296

QUERY: 390 NEGVDEDISSLFIEDSARKTLA 412
| | + | | +++ + | ++
SBJCT: 297 NRYGTAKVIGRLYVKQPLKATIS 319

SCORE = 41.3 BITS (96), EXPECT = 0.047
IDENTITIES = 43/174 (24%), POSITIVES = 70/174 (39%), GAPS = 11/174 (6%)

QUERY: 243 CAVHGDLRPPPIIWK--RNGLTLNF--LDLEDINDFGEDDSLYITKVTTIHMGNYTCHASG 298
| + | | | + | | + | | | | | | | |
SBJCT: 711 CSAEGYPVPTIVWFKSGAGVPPQFQPIALNGRIQVLSNGSLLIKHVVEEDSGYYLCKVSN 770

QUERY: 299 H--EQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVST 356
+ + + | | + | | + | | | | + | | ++
SBJCT: 771 DVGADVSKSMYLTVKIPAMITSYPNTTLATQGQKKEMSCTAHGEKPIIVRWEKEDRIINP 830

QUERY: 357 QMSKQLSLLANGSELHISSVRY-----EDTGAYTCIAKNEGVDEDISSLFIED 405
+ | ++ | | | | ++ | | + | | | | | ++
SBJCT: 831 EMARYLVSTKEVGEEVISTLQILPTVREDSGFFSCHAINS YGEDRGIIQLTVQE 884

SCORE = 40.6 BITS (94), EXPECT = 0.074
IDENTITIES = 46/165 (27%), POSITIVES = 69/165 (40%), GAPS = 7/165 (4%)

QUERY: 243 CAVHGDLRPPPIIWKRNGTLNFLDLEDINDFGEDDSLYITKVTT-IHMGNYTCHASGHEQ 301
| | | | | + | | + | + + | + | | | + |
SBJCT: 525 CRVIGYPYYSIKWYKNSNLLPFNHRQVA--FENNGTLKLSDVQKEVDEGEYTCNVLVQPQ 582

QUERY: 302 LFQTHVLQVN--VPPVIRVYPESQAQEPGVAASLRCHAEGIPMP-RITWLKNGVDVSTQM 358
| + + | | | + | | + | | | | | + | +
SBJCT: 583 LSTSQSVHVTVKVPPFIQPF-EFPRFSIGQRVFIPCVVSGDLPITITWQKDGRIPIGSL 641

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEGVDEDISSLFI 403
+ + | | | ++ | | | | + | | | +
SBJCT: 642 GVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAVEHQSQLIV 686

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Homo sapiens* (SWISSPROT Acc:Q13449) (SEQ ID NO:58) (Table 2O).

Table 2O. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (SEQ ID NO:58)

PTNR:SWISSPROT-ACC:Q13449 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR (LSAMP) - HOMO SAPIENS (HUMAN), 338 AA.

LENGTH = 338

SCORE = 191 (67.2 BITS), EXPECT = 6.7E-12, P = 6.7E-12
IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

The amino acid sequence of the FCTR2 protein has 68 of 190 amino acid residues (35%) identical to, and 92 of 190 residues (48%) positive with Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SPTREMBL Acc:O70246) (SEQ ID NO:59) (Table 2P).

Table 2P. BLASTP of FCTR2 against Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SEQ ID NO:59)

PTNR:SPTREMBL-ACC:O70246 PUTATIVE NEURONAL CELL ADHESION MOLECULE (PUNC)
(PUTATIVE NEURONAL CELL ADHESION MOLECULE, SHORT FORM) - MUS MUSCULUS
(MOUSE), 793 AA
LENGTH = 793
SCORE = 203 (71.5 BITS), EXPECT = 7.0E-12, SUM P(2) = 7.0E-12
IDENTITIES = 68/190 (35%), POSITIVES = 92/190 (48%)

The amino acid sequence of the FCTR2 protein has 58 of 199 amino acid residues (29%) identical to, and 91 of 199 residues (45%) positive with CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SPTREMBL Acc: O02869) (SEQ ID NO:60) (Table 2Q).

Table 2Q. BLASTP of FCTR2 against CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SEQ ID NO:60)

PTNR:SPTREMBL-ACC:O02869 CHLAMP, G11-ISOFORM PRECURSOR - GALLUS GALLUS
(CHICKEN), 350 AA.
LENGTH = 350
SCORE = 191 (67.2 BITS), EXPECT = 7.7E-12, P = 7.7E-12
IDENTITIES = 58/199 (29%), POSITIVES = 91/199 (45%)

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SWISSPROT Acc:Q62813) (SEQ ID NO:61) (Table 2R).

Table 2R. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SEQ ID NO:61)

PTNR:SWISSPROT-ACC:Q62813 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR
(LSAMP) - RATTUS NORVEGICUS (RAT), 338 AA.
LENGTH = 338
SCORE = 188 (66.2 BITS), EXPECT = 1.5E-11, P = 1.5E-11
IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

FCTR2 protein has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and

reproductive physiology. Frazzled encodes a Drosophila member of the DCC immunoglobulin subfamily and is required for CNS and motor axon guidance (Cell 87:197-204(1996)).

Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP) and cloning and sequence of the human homologue is described in Eur. J. Biochem. 225:937-946(1994). This protein may modulate the action of some growth factors on cell proliferation and differentiation. FRP binds heparin. The follistatin-related protein is a secreted protein and has one follistatin-like domain. The cloning and early dorsal axial expression of Flik, a chick follistatin-related gene and evidence for involvement in dorsalization/neural induction is presented in Dev. Biol. 178:327-342(1996). Roundabout controls axon crossing of the CNS midline and defines a novel subfamily of evolutionarily conserved guidance receptors, as shown in Cell 92:205-215(1998). cDNA cloning and structural analysis of the human limbic-system- associated membrane protein (LAMP) is described in Gene 170:189-195(1996). LAMP, a protein of the OBCAM family that contains three immunoglobulin-like C2-type domains, mediates selective neuronal growth and axon targeting. LAMP contributes to the guidance of developing axons and remodeling of mature circuits in the limbic system. This protein is essential for normal growth of the hippocampal mossy fiber projection. LAMP is attached to the membrane by a GPI-Anchor. It is expressed on limbic neurons and fiber tracts as well as in single layers of the superior colliculus, spinal chord and cerebellum. Characterization of the human full-length PTK7 cDNA encoding a receptor protein tyrosine kinase-like molecule closely related to chick KLG is disclosed in J. Biochem. 119:235-239(1996). Based upon homology, FCTR2 proteins and each homologous protein or peptide may share at least some activity.

Functions and therapeutic uses:

The OMIM gene map has identified this region which the invention maps to (5q21-5q31) as associated with susceptibility to the following diseases (OMIM Ids are underlined):

- Allergy and asthma
- Hemangioma,
- capillary infantile Schistosoma mansoni infection, susceptibility/resistance to Spinocerebellar ataxia
- Bronchial asthma
- Plasmodium falciparum parasitemia,
- intensity of Corneal dystrophy, Groenouw type I, 121900; Corneal dystrophy, lattice type I, 122200;
- Reis-Bucklers corneal dystrophy; Corneal dystrophy, Avellino type Eosinophilia, familial Myelodysplastic syndrome;

- Myelogenous leukemia, Acute Cutis laxa, recessive, type I, Deafness, autosomal dominant nonsyndromic sensorineural, 1 Contractural arachnodactyly, Congenital Neonatal alloimmune thrombocytopenia;
- Glycoprotein Ia deficiency Male infertility;
- Charcot-Marie-Tooth neuropathy, Demyelinating Gardner syndrome ;
- Adenomatous polyposis coli;
- Colorectal cancer;
- Desmoid disease, hereditary, 135290;
- Turcot syndrome,276300;
- Adenomatous polyposis coli, attenuated
- Colorectal cancer

Therefore the invention is implicated in at least all of the above mentioned diseases and may have therapeutic uses for these diseases.

This sequence has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Therefore the invention is also implicated in disorders such as or therapeutic uses for:

- Neurodegenerative disorders, nerve trauma, epilepsy, mental health conditions
- Tissue regeneration in vivo and in vitro

Female reproductive system disorders and pregnancy

FCTR3

FCTR3, is an amino acid type II membrane, neurestin-like protein. The FCTR3a nucleic acid of 1430 nucleotides (also designated 10129612.0.118) is shown in Table 3A. An ORF was identified beginning with an ATG initiation codon at nucleotides 69-71 and ending with a TAG codon at nucleotides 1212-1214. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3A, and the start and stop codons are in bold letters.

Table 3A. FCTR3a Nucleotide Sequence (SEQ ID NO:5)

AAAAAAGGCGGGGGTGGACTTAGCAGTGTAATTTGAGACCGGTGGTAAGGATTGGAGCGAGCTAGAGATGCTGCACGCTGCTAACA
 AGGGAAGGAAGCCTTCAGCTGAGGCAGGTCGTCCCATTCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCT
 CCCATAATCCTCCACAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGG
 AATTCTCCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGT
 CGACTCTGAGGCCCCCTCTCCACCCCCCTCACAACCACACGCTGTCCCATCACTCGTCCGCCAACTCCCTCAACAGGAACTCAC
 TGACCAATCGGCGGAGTCAGATCCACGCCCCGCCCCAGCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCTCAGCTTCAGGACA
 GCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCTCTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCAGCAGCT

CTTCCCCGGGATACCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCAGGAATACTTTCTCCAGGAAGGCTT
TCAAGCTGAAGAAGCCCTCCACTGTCAGCTGGAAATGTGCTGCCCTCTCCGCCATCGCGGCCCTCTCTGGCTATTTTGC
TGGCGTATTTTCATAGTGCCCTGTTGAAAAACAGCAGCATAGACAGTGGTGAAGAGTTGGTCGGCGGGTAACACAAGAAG
TCCCACCAGGGGTGTTTTGGAGGTACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTC
TCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGA
GTGTGGTTGAGTCTCCAGGGAACGCCGAGCATAACAGACCTTGGTTCAGAATGAAGCCGTGTTGTGCAGTACCTGGATGTGGGCC
TGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTTTCTTCAATACTGTGTCTAGATGGGACCATCTAGTTGC
AGAAAAACAAGCTCAGGGCGCCCACTGATTGACATTATGATTGAGTGCAGGACTGTCCACGTAAGTCCCATGGGAATGGTGAATGT
GTGTCCGGGTGTGTCACTGTTTCCAGGATTTCTAGGAGCAGACTGTGCTAAAGACCTTCTGCCTTGACTTCTGCAAGACAATC
ATTAATAAAGCTGCTCTGTAAATACTAAAAAAAACA

The FCTR3 polypeptide (SEQ ID NO:5) encoded by SEQ ID NO:5 is 381 amino acid residues and is presented using the one-letter code in Table 3B.

Table 3B. Encoded FCTR3a protein sequence (SEQ ID NO:6).

MLHAANKGRKPSAEAGRPIPTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGP
PNHHSQSTLRPPLPPPHNHTLSHHSSANSLSNRSLTNRRSQIHAPAPAPNDLATTPEVQLQDSWVLSNVPLETRHFLFKTSSGS
PLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKKPKSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVG
RRVTQEVPPGVFWRSQIHISQPQFLKFNISLGDALFGVYIRRLPSPHAQYDFMERLDGKEKWSVSPRERRSIQTLVQNEAVFV
QYLDVGLWHLAFYNDGDKEMVSFNTVLDGTI

In an alternative embodiment, the 5' end of the FCTR3a nucleic acid could be extended as it is in the 9826bp FCTR3b (also referred to herein as 10129612.0.405) shown in Table 3C. An ORF was identified beginning with an ATG initiation codon at nucleotides 280-282 and ending with a TAA codon at nucleotides 8479-8481. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3C, and the start and stop codons are in bold letters. Italicized bases 1-201 refer to a variable 5' region that will be further discussed below.

Table 3C. FCTR3b Nucleotide Sequence (SEQ ID NO:7)

TTAAATCCTCATACCTTAAAGGAGATGTGTATATAAGGGAGTTGGAACCAGCATTAGATGAGTTGACAAAAATGCAGTT
TCAGTTCTAGAGGTCTGGGAAGTCCAAGAAACAGGTGCTGGCAGATTGGATTCCCCGTGAGGGCTTTCTTCTGGCTTGA
AGTTGGCTGCTTCTGCTGAGACTTCTCATGGCAGAGACTGAGGGTGGCAAAGTGACAAGTGCCAAAACCTCAGGCCTGA
CTTTCTGAAAAACATCAGCATTTCTGCCATATCTGGAATAATGGATGTAAAGGACCGCGACACCGCTCTTTGACCAGAGG
ACGCTGTGGCAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACAGAAATCCTACA
GCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACCGG
GAGTCAGATGAGTTTCTAGACAAGGAACCAACTTACCCTTGCCGAACCTGGGCATCTGTGAGCCCTCCCCACACCGAAG
CGGCTACTGCTCCGACATGGGGATCCTTACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGG
GAGGGATGTCTCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTCTGT
GAAAACCTCGGCCCTTACCCTGACTGACTCTGACAACGAAACAAATCAGATGATGAGAACGGTCTGTCCTTCCACCTAC
ATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGTCTCCATAATCCTCCACAGTTAGCTGCCAGATGCCATTGC
TAGACAGCAACACCTCCCATCAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCA
TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACACAGCCAGTCTGAGGCCCCCTCTCCACC
CCCTCACAAACACACGCTGTCCCATCACCCTCGTCCGCCAATCCCTCAACAGGAACCTACTGACCAATCGGCGGAGTC
AGATCCACGCCCCCGCCCCAGCGCCCAATGACCTGGCCACCACACAGAGTCCGTTTCTGAGTCTCAGGACAGCTGGGTGCTA
AACAGCAACGTGCCACTGGAGACCGGCACTTCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCTCAGCAGCTCTTCT
CCCCGGATACCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCGCTGCTGCCAGGAATACTTTCTCCAGGAAGG
GTTTCAAGCTGAAGAAGCCCTCCAAATCTGACAGTGGAAATGTGCTGCCCTCTCCGCCATTGCGCGGGCTCCTCTTG
GCTATTTTCTGCTGGCGTATTTTCATAGTGCCCTGGTTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCG
GCGGGTAACACAAGAAGTCCACAGGGGTGTTTTGGAGGTCAAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCA
ACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCCAGTATGACTTC
ATGGAACGTCTGGACGGGAAGGAGAAGTGAGTGTGGTTGAGTCTCCAGGGAACGCCGAGCATAACAGACCTTGGTTCA
GAATGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGA
TGGTTTCTTCAATACTGTTGTCTAGATTGAGTGCAGGACTGTCCACGTAAGTCCATGGGAATGGTGAATGTGTGTCC
GGGTGTGTCACTATTTCCAGGATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGG
ACAATATTTCTAAAGGACGTGCCAGTGTACAGCGGCTGGAAGGTGCAGAGTGCAGCTGCCATGAATCAGTGCATCG
ATCCTTCTGCGGGGCCACGGCTCCTGCATTGATGGGAACGTGTCTGTCTGCTGGCTACAAAGGCGAGCACTGTGAG

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GAAGTTGATTGCTTGGATCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGG
TGGTCTGAAGTGTGAGCTGGGCTGGTCCAGTGCCAGACCACTGTCAGTGGGCATGGTACCTGCTGACACGGGCC
CTGGCAGGTCCGATGCCAACAAGTGGGTCCCGACTGCTGTGAAGTGTGCTCAGTCTGTGGCACTACAGGGCTC
TGCATCGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCGCTGCAT
TGAGCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAA
CGGCAGGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGGCAG
TGTGTCTGCCAGACCGGTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCCTGTGCTGATAACAAGGATAATGA
GGGAGATGGCCTGGTGGATTGTTTGGACCTGACTGCTGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGGT
CCCCGGACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCCGAGTGAAGTCTTCTATGACCGTATCAAGCTC
TTGGCAGGCAGGATAGCACCCACATCATTCCTGGAGAGAACCTTTCAACAGCAGCTTGGTTCTCTCATCCGAGGCCA
AGTAGTAACCTACAGATGGAATCCCCTGGTGGTGTGAACGTGCTTTTTGTCAAGTACCCAAATACGGCTACACCATCA
CCCGCCAGGATGGCACGTTTCGACCTGATCGCAAATGGAGGTGCTTCTTGACTCTACACTTTGAGCGAGCCCGTTTCATG
AGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTGGTGTATGAAGACCGAGGAGAACTC
CATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTG
CTGCCCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCGAATGTGAAA
CTTCGCTATCTGAGCTCTAGAAGTGCAGGGTACAAGTCACTGTGAAGATCACCATGACCCAGTCCACAGTGCCCTGAA
CCTATTAGGTTTCACTTGTGGTGGCTGTGCGAGGAGCACTCTTCCAGAAGTCACTCCAGGCTTCCCAACCTCCGCT
CCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTCCGGTTT
GAATATGAGACCTGTCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTGAGCTGGACCCCTCCAA
CCTCGGTGGCTGGTCCCTAGACAAAACACCACATCCTCAATGTTAAAGTGAATCCTACACAAAGGCACTGGGAAAACC
AGTTCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGCAATGGTCCGCCCGGAGCATTTCTGTCCAGCTGC
AACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGA
CTTCAATTACATCCGACGATCTTTCCCTCTCGAAATGTGACCAAGCATCTTGAGTTACGAAATAAGAGTTTAAACATA
GCAACAACCCAGCACACAAAGTACTACTTGGCAGTGGACCCGCTGCGGCTCGCTCTACGTGTCCGACACCAACAGCAGG
AGAATCTACCGCGTCAAGTCTCTGAGTGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCA
GTGTCTACCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTG
CAGTAGACAAGAATGGGCTCATGTACTTTGTGCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCCACC
CTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGTGGA
GTGGCCAAACAGACCTTGCTGTCAATCCCATTGGATAACTCCTGTATGTTCTAGAGAAACAATGTATCCTTCGAATCACC
GAGAACCAACCAAGTCAGCATATTGCGGGACGCCCATGCACTGCCAAGTTCTTGGCATTGACTACTCACTGACGAACTA
GCCATTCACTCTGCCCTGGAGTCAGCAGTGGCATTGCCATTTCTACACTGGGGTCTCTACATCACTGAGACAGATGA
GAAGAAGATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACT
GCAAAAACGATGTCAATTGCAACTGCTATTGAGGAGATGATGCCTACGCGACTGATGCCATCTGAAATCCCCATCATCC
TTAGCTGTAGCTCCAGATGGTACCATTACATTGCGAGACCTTGGAATATTTCGATCAGGGCGGTGAGCAAGAAACAAGCC
TGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCC
ACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAATTG
ATTGACAATAATGGGAATTCCTGAAGATCCGTCCGGACAGCAGTGGCATGCCCGTCACTGTCTATGCCCTGACAACCA
GATCATCACCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCT
ATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGC
CGCCTGACCAACGTGACGCGCCCCACGGGGTGGTAACCAGTCTGCACCGGGAATGGAGAAATCTATTACCATTGACAT
TGAGAACTCCAACCGTGATGATGACGTCACTGTATCACCAACCTCTCTTCAGTAGAGGCCTCTACACAGTGGTACAAG
ATCAAGTTCGGAACAGCTACCACTCTGTAATAATGGTACCCTGAGGGTGTATGTATGCTAATGGGATGGGTATCAGCTTC
CACAGCAGCCCCATGTCTAGCGGGACCATCACCCCACTTGGACGCTGCAACATCTCCTGCTATGAGCTTACAGATTG
CTTAAACTCCATTGAGTGGCGCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCC
ATGGAAGAAATCTCTTGCTCATTGACTATGATCGAAATATTGCGACTGAAAAGATCTATGATGAACACCGGAAGTTACC
CTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCTCTGGCTGCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCTATA
CTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGATCG
TGTCCCGCATGTTTCGTGACGGGAAAGTGTGGAGCTACTCTACCTTGACAAGTCCATGGTCTCTCTGCTTCAGAGCCAA
CGTCAGTATATATTGAGTATGACTCTCTGACCCGCTCTGCGCTCACCATGCCCAGCGTGGCCCGGACAGCATGTG
CACACACCTCCATCGCTACATCCGTAATATTACAACCTGCAAGCAATGCTTCGTTCACTCTTGTACTACAGTG
ATGACGGCCGCATCCTGAAGACCTCCTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAGTTA
TCAGAGATTGTCTACGACAGTACCGCGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCA
AAGTGGGGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGG
AAGGCATGGTCAATGCCAGGTTTGACTACCTTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGT
GAGACTCCCCCTCCCGTTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAAGTTTGGAGTCAT
CTATTATGACATCAACAGATCATCACCACTGCGGTGATGACCTCAGCAAACTTCGACACCCATAGGCGGATCAAGG
AGGTCAGTATGAGATGTTCCGGTCCCTCATGTACTGATGACGGTGCAATATGACAGCATGGCGAGGTTGATCAAGAGG
GAGCTAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCGAGCTCCAGAGCGTGGC
CGTCAATGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGC
GCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGAGCATGGC
TATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCGAAGGGCTCCTAACAAGAGCCTACAACAAGGCCAGCGG
GTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGCCACCACCTGCAGTACT
TCTACTCTGACCTCCACAACCCGACGCGCATCACCATCTTACAATCACTCAACTCGGAGATTACCTCACTGTACTAC
GACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGCGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCC
TCTGGCTGTGTTGAGCATCAACGGCCTCATGATCAAAACAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCA
ACCCGACTTCCAGATGGTCATTGGCTTCCATGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGT
GATTATGATGTGCTGGCAGGACGATGGACCTCCCGAGCTATACCATGTGAAAAACGTGGGCAAGGAGCCGCGCCCTT
TAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAAGTATTGAAGAACTACGTGACAGATGTGAAAAGCT
GGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTTCCGAGAGCCAAAATGTATTTCTGTGCTCCTCCC
TATGAATTGTGAGAGTCAAGCAAGTGAGAAATGGACAGCTATTACAGGTGTCCAACAGACAACAGAGAGACATAACCA

GGCCTTCATGGCTCTGGAAGGACAGGTCTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTG
 CCACCACCACGCCCATCATTTGAGGCATCATGTTTGCCATCAAAGAAGGGCGGGCACGGGCGTGTCCAGCATC
 GCCAGCGAAGATAGCCGCAAGCATCTGTGCTGAACAACGCCCTACTACCTGGACATGCACTACAGCATCGAGGG
 CAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACTAGGCACCACCATCGGCCGCAAGG
 5 TGCTAGAGAGCGGGGTGAACGTGACCGTGTCCAGCCCAGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAACATT
 GAGTTCAGTACTCCACGTGCTGCTCAGCATCCGCTATGGCCTACCCCGACACCCTGGACGAAGAGAAGGCCCGCGT
 CCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGA
 GCCGCCTGTGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGGTGCAAGGGTACGAGGGATATTACGTGCTT
 CCCGTGGAGCAATACCCAGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTAAAGACAGAATGAGATGGGAAAGAGGTA
 10 ACAAAATAATCTGCTGCCATTCCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCTCTCTCTAAGGAGATGAAGAC
CTAACAGGGGCACTGCGCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGTAGTTCAAATGCTACT
GTCCAAGCGAGAAGTCCCTCATCTGAAGTAGACTAAAGCCCGCTGAAAATTCGAGGAAAACAAAACAAACGAATGAA
TGAACAGACACACAAATGTTCCAAGTTCCTTAAATATGACCCACTTGTCTGGGTCTACGCAGAAAAGAGACGCAAA
 15 GTGTCCAAAAGGAACAAAAGAAACAAAACGAATAAGCAAAGAAGAAACAAAACAAAACAAAACAAACACACGGA
CCGATAAACAAAGAAGCGAAGATAAGAAAGAAGGCCTCATATCCAATTACCTCACTCATTACATGTGAGCGACACGCAG
ACATCCGCGAGGGCCAGCGTCACAGACCAGCTGCGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACAT
TTTCGTTTAAAGCAAAATACAGGTGCATTTAAAAACAGCACTTTGGGGGTGATTGTGTGTAGCGCTGGGGAGGGGGGATAA
AAGAGGAGGAGTGAGCACTGGAATACTTTTAAAGAAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAATCA
 20 AAGTGAATAATACCATCCAGCACTTAAGTCTCAGGTCCCACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGT
GTAAAATTTAATTCAAAATGGTGGCTATAATCACTACAGATAAATTTCTACTCTTTTGTCTTTGGAGATTCCATTGTGG
ACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGTATCAGTTTCGGTAGAGGTGCAGCATC
GTGACACTTTTGCTAACAGGTACCACTTCTGATCACCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATT
TAAAATTTAGTGTGTTTGTGTTGGTCCGAAACTGAGACAATCACATGACAGTCACCACGAGGAGAGAAAATTTAAAAA
 25 ATAAAAAATAAAAAACAAAATAATTTTAAAAATAAAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAACCTT
TTTGTAAATATACATGTATGAATTGTTTCATCGAGTTTTTATATTAATTTTAAATTTGCTGCTAAGCAAAGACTAGGGACAGG
CAAAGATAATTTATGGCAAAGTGTTTAAATGTTTATACATAAATAAAGTCTCTAAACTCCTGTG

The FCTR3b polypeptide (SEQ ID NO:8) encoded by SEQ ID NO:7 is 2733 amino acid
 residues and is presented using the one-letter code in Table 3D. The protein has a predicted
 30 molecular weight of 303424.3 daltons.

Table 3D. Encoded FCTR3b protein sequence (SEQ ID NO:8).

MDVKDRRHRSLSLTRGRCGKECRYTSSSLDSEDCRVPTQKYSYSSSETLKAYDHDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAEIGI
 CEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLDSDNENKSDDENGRPI
 PTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTPNDEEFSPNSYLLRACSGPQQASSSGPPNHSQSTLRPPLPPPHNH
 35 TLSHHHSSANSLSNRNSLTNRSSQIHAPAPAPNDLATTPEVQLQDSWVLNSVPLETRHFLFKTSSGSTPLFSSSPGYPLTSGTV
 YTPPRLPRNTFSRKAFKLKPSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRRTVQEVPPGVFWRSQI
 HISQPQLKFNISLKGKDALFGVYIRRGLPPSHAQYDFMERLDGKEKWSVESPRRRSIQTLVQNEAVFVQYLDVGLWHLAFYNDG
 KDKEMVSFNTVVLDSVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAAACPVLCSGNGQYKGTCCQCYSGWKGAECVPMNQCIDP
 40 SCGGHGSICIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYPDPDTGLCSCDPNW
 MGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQVRCHPRCIEHGTCCKDGKCECREGWNGEHCTIGRQTAGTETDGCPLCN
 GNGRCTLGQNSWQVCVQCTGWRGPGCNVAMETSADNKNDEGDLVCLDPCCLQSACQNSLLCRGSRDPLDI IQQGQTDWPAVKS
 FYDRIKLLAGKDSLTHIPGENPFNSSLVSLIRGVVTTDGPLVGVNVSFVKYPKYGYTITRODGTDLIANGGASLTLHFERAPF
 45 MSQERTVWLPWNSFYAMDITLVMKTEENSIPSCDLSGFVRDPII ISSPLSTFFSAAPGQNPVIVPETQVLHEEIELPGSNVKKLYLS
 SRTAGYKSLKLTMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQVRVYGLSDAVSVGFYETCPSLILW
 EKRTALLQGFELDPNSLGGWSLDKHHILNVKSGILHKGTTGENQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAV
 GIDGSLYVGDFNYIRRIIPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIRYVKSLSGKTDLAGNSEVVAG
 50 TGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEW
 TDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCCQVPGIDYSLSKLAHSALESASAIASHTGVLYITETDEKKINLRQ
 VTTNGEICLLAGAASDCCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNFAFNQYEAASPG
 EQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVTGNGGLKVVSTQNL
 ELGLMTYDNGTGLLATKSDGTGTTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSIITIDIENSNRDDVTVINLSSVEASYTVVQ
 55 DQVRNSYQLCNNGTLRVMYANGMGISFHSPEHVLGTTIPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLL
 SIDYDRNIRTEKIYDDHRKFTLRIIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERDIDKQGRIVSRMFADGKVS
 YSYLDKSMVLLQLSQSQRYIFEYDSSDRLLAVTMPVSVAHMSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRIKLSFLGTGRQV
 60 YKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSGGFSTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTHDNSFRIASIKP
 VISETPLVDLYRYDEISGKVEHFGKFGVIYDINQIITTAVMTLSKHFDTHGRKEVQYEMFRSLMYWMTVQYDSMGRVIRKELK
 LGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLNHLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDI
 FEYNSKGLLTRAYNKASGWSVQYRYDGVGRASYKTNLGHHLQYFYSDLHNPTRI THVYNHSNSEITSLYYDLQGHLFAMESSSGE
 EYVVASDNTGTPLAVFSINGLMIKQLQYTAIGEIIYDSNPDPQMVGIFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVG
 KEPAPFNLVYFKSNPLSSELDLKNYVTVKSWLVMFGFLSNIIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQ
 AFMALEGQVITKKLHASIREKAGHWFATTPPIIGKIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYF
 VKIGSADGDLVLTGTTIGRKVLESGVNVTVSQPTLLVNGRTRFRFTNIEFYQSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTA
 WAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMGRK

In further alternative embodiments the italicized bases in the 5' end of the FCTR3b sequence in table 3C is a variable region. This region can be substituted for in other embodiments of FCTR3. The nucleotide sequence for 9823bp FCTR3c (also referred to herein as 10129612.0.154) has the same nucleotide sequence as FCTR3b except that the italicized region is replaced with the 201 base sequence shown in Table 3E. An ORF for the total FCTR3c nucleotide sequence was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3c. This open reading frame will translate the same amino acid sequence as shown in Table 3C for FCTR3b.

Table 3E. Encoded FCTR3c 5'end nucleotide sequence (SEQ ID NO:9).

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTCTAGGGAGCGAAGCTACTGACCGA
GCTGCTGTTACATCCAGCTTTTAAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3F to form 9823bp FCTR3d (also referred to herein as 10129612.0.67). An ORF was identified beginning with an ATG initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3d. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3F. Encoded FCTR3d 5'end nucleotide sequence (SEQ ID NO:10).

GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTCTAGGGAGCGAAGCTACTGACCGA
GCTGCTGTTACATCCAGCTTTTAAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3G to form 9765 bp FCTR3e (also referred to as 10129612.0.258). An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8408-8410. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3e. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3G. Encoded FCTR3e 5'end nucleotide sequence (SEQ ID NO:11).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA
TTCTGCTACAACTATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAA

ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCTTGGCATTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCT
 GGAGTCAGCCAGTGCCATTGCTCTCTCACACTGGGGTCTCTACATCACTGAGACCTGAGAAGAAGATTAAACCGTC
 TACGCCAGGTAACAACCAACCTGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTCTGCAAAAACGATGTCAAT
 TGCAACTGCTATTTCAGGAGATGATGCCCTACGCGAGTACTGACCTTTGAATTCCTCCATCATCTTGTAGCTGCCAGA
 5 TGGTACCATTACATTGCAGACCTTGGAAATATTCGGATCAGGGCGGTGACGCAAGAACAAGCCTGTTCTTAATGCCCTTCA
 ACCAGTATGAGGCTGCATCCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC
 CTGGTGACAGGGGAGTACTTGTACAATTCACATATAGTACTGACAATGATGCTCACTGAATTGATTGACAATATGGGAA
 TTCCCTGAAGATCCGTGCGGACAGCAGTGGCATGCCCGCTCACCTGCTCATGCTGACAACCAGATCATCACCTCACC
 10 TGGGCACCAATGGAGGCCCTCAAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG
 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTCGAC
 CGCCCCACGGGGTGGTATGACCTGTGCACCGGGAAATGGGAAATCTATTACCATTGACATTGAGAATCCCAACCGTG
 ATGATGACGTCACGTGCATCACCAACCTCTCTTCACTAGAGGCTCTACACAGTGGTACAAGATCAAGTTCGGAACAGC
 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGT
 CCTAGCGGGACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGT
 15 GGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG
 TCCATTGACTATGATCGAAATATTGGAGCTGAAAAGATCTATGATGACCACCGGAAGTTCACCTGAGGATCATTTATGA
 CCAGGTGGGCTACCGCCCTCTCTGGCTGCCAGCAGGGCTGGCAGCTGTCAACGTGTCATACTTTCTCAATGGGCGC
 TGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGATCGTGTCCCGCATGTTTCGCT
 GACGGGAAAGTGTGGAGCTACTCTACCTTGACAAGTCCATGGTCTCTCTGCTTCAAGGCCAACGTGAGTATATATTTGA
 20 GTATGACTCCTCTGACCGCTCTTGGCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCG
 GCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTATGACGGCCGATCCTG
 AAGACCTCCTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAGTTATCAGAGATTGTCTACGA
 CAGTACCGCCGTCACTTTCGGGTATGACGAGACCACTGGTGTCTGAAGATGGTCAACCTCCAAAGTGGGGCTTCTCT
 GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGAGCAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC
 25 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCTCCCGT
 TGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC
 AGATCATCACCACTGCCGTGATGACCTCAGCAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG
 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACCTGGGGCC
 CTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCGCA
 30 CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTACTGAAACCCAGGCAACAGTGTGGCCCTCATGCCCTTGGC
 TATGACCTCCGGGATCGGATAACACAGCTCGGGGATGTGCAATGCAAAATTGACGACGATGGCTATCTGTGCCAGAGAGG
 GTCTGACATCTTGAATACAATTCGAAGGGCTCTTAACAAGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCCAGTACC
 GCTATGATGGCGTAGGACGGCGGGCTTCTTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC
 AACCCGACGCGCATCACCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTACTAGACCTCCAGGGCCACCT
 35 CTTTGGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCTCTGATAACACAGGGACTCCTCTGGCTGTGTTTCA
 TCAACGGCCCTCATGATCAACAGCTGCAGTACACGGCTATGGGGAGATTTATATGACTCCAACCCCGACTTCAGATG
 GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGTATGATGATGCTGGC
 AGGACGATGGACCTCCCCAGACTATACCATGTGGAAGAACGTTGGGCAAGGAGCCGGCCCCCTTAACTGTATATGTTCA
 40 AGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAGCTGGCTTGTGATGTTTGA
 TTTTCACTTAGCAACATCATCTCTGGCTTCCCGAGAGCCAAATGTATTTCTGTCCTCCTCCCTATGAATTGTGAGAG
 TCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACAGGCGCTTCATGGCTCTGG
 AAGGACAGGTCACTACTAAAAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC
 ATTTGGCAAAGGCATCATGTTTGGCATCAAAGAAGGGCGGTGACCAAGGGCGTGTCCAGCATCGCCAGCAAGATCCCG
 45 CAAGGTGGCATCTGTGTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACCCACTACT
 TTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGTG
 AACGTGACCGTGTCCCAGCCCAGCTGTGCTGGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCCAGTACTCCAC
 GCTGCTGTGCTCAGCATCCGTATGGCCTCACCCCCGACACCTGGACGAAGAGAAGGCCCGCTCTGGACCAGCGGAGAC
 AGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCTGTGGACTGAG
 GCGGAGAAGCAGCAGCTTCTGAGCACCGGGCGGTGCAAGGATACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCC
 50 AGAGCTTGCAGACAGTGAAGCAACATCCAGTTTTTAAGACAGAAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGC
CATTCTTGTCTGAATGGCTCAGCAGGAGTAACTGTTATCTCTCTCTAAGGAGATGAAGACCTAACAGGGGCACTGCG
GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGGATTCAAATGCTACTGTCCAAGCGAGAAGTCC
CTCATCTGAAGTAGACTAAAGCCCGCTGAAAATTCGAGGAAAACAAAACAAACGAATGAATGAACAGACACACAA
 TGTTCGAAGTTCCCCTAAAATATGACCCACTTGTCTGGGTCTACGCAGAAAAGAGACGCAAGTGTCCAAAAGGAACAA
 55 AAGAACAACAAACGAATAAGCAAAGAAGAAACAAACAAACAAACAAACACACCGGACCGGATAAACAAAGAAGC
 GAAGATAAGAAAGAGGCGCTCATATCCAATTACCTCACTTACATGTGAGCGACACGCAGACATCCCGGAGGGCCAG
 CGTCAACGACAGCTGCGGGACAAACCACTCAGACTGCTTTAGGACAAATACTTCTGACATTTTCGTTTGAACAAATA
 CAGGTGCATTTAAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCTGGGGAGGGGGGATAAAAGAGGAGGAGTGAGCA
 60 CTGGAAATACTTTTTAAAGAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAAATCAAAGTGAATAATACCAT
 CCAGCACTTAACCTCTCAGGTCCCACTAAGTCTGGCCTGAGCTAATTTATTGAGCGCAGAGTGATAAATTTAATTCAAA
 ATGGTGGCTATAATCACTACAGATAAATTTCACTCTTTTGTCTTTGGAGATTCCATTGTGGACAGTAATACGCAGTTA
 CAGGGTGTAGTCTGTTTAGATTCCGTAGTTCTGTGGGTATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAAC
 AGGTACCACCTCTGATCACCTGTACATACATGAGCCGAAGGCAACATCACTGTTTCAGATTAAATTTATAGTGTGT
 65 TTGTTTGGTCCAGAACTGAGACAATGACATGACAGTCACCAAGGAGAGAAAATTTAAAAAATAAAATAAAAACAAA
 AAAAAATTTAAAAATTAATAAAACAAAAATAAAGTCTAATAAGAACTTTGGTACAGGAACCTTTTGTAAATATACATGTA
 TGAATTGTTTCATCGAGTTTTTATATTAATTTAATTTGCTGCTAAGCAAGACTAGGGACAGGCAAGATAATTTATGGC
 AAAGTGTTTAAATGTTTTATACATAAATAAAGTCTCTAAAACCTCTGTG

The FCTR3f polypeptide (SEQ ID NO:13) encoded by SEQ ID NO:12 is 2724 amino acid residues long and is presented using the one-letter code in Table 3I. This sequence differs from FCTR3b in that it is missing amino acids 758-766 from that polypeptide.

Table 3I. Encoded FCTR3f protein sequence (SEQ ID NO:13)

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5 MDVKDRRHRSILTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHSRMHYGNRVTDLIHRESDEFPRQGTNFTLAEIGI
CEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRRSSGLSSRENSALTLTDSNENKSDDENGRPI
PTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNH
TLSHHHSSANSILNRNSLTNRRSQIHAPAPAPNDLATTPEVQLQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTV
10 YTPPPRLLPNTFSTRKAFKLKPKSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRRVTVQEVPPGVFWRSQI
HISQPFQKFNISLKGKDALFGVYIRRGLPSSHAQYDFMERLDGKEKWSVSPRERSIQTLVQNEAVFVQYLDVGLWHLAFYNDG
KDKEMVSFNTVVLDSDVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCCQYSGWKGAECDVPMNQCIDP
SCGGHGSIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCPGWGGLNCELARVQCPDQCSGHGTYPDPDTGLCSDPNW
MGPDCSVEVCSVDGCTHGVCIIGACRCEEGWTGAACDQVRCHPRCIEHGTCCKDGKCECREGWNGEHCTIDGCPDLNNGRCTLGQ
15 NSWQCVCQGTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPCCLQSACQNSLLCRGSRDPLDI IQQGQTDWPAVKSFYDRIKLLA
GKDSTHIIPGENPFNSSLSLIRGQVVTDTGTPLVGVNVSFVKYPKYGYTITRQDGTDFDIANGGASLTLLHFERAPFMSQERTVWL
PWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDI I ISSPLSTFFSAAPGQNP IVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSL
LKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLILWEKRTALLQG
FELDPSNLGGWSLDKHHILNVKSGILHKGTEGENQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVG
20 DFNIRIRIFPSRNVTSILELRNKEFKHSNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFD
EARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMD
NSLYVLENNVILRITENHQVSI IAGRPMHCQVPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINRLRQVTTNGEICL
LAGAASDCDCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPEGEQELVFN
DGIHQYTVSLVTGEYLYNFTYSTDNDVTELDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLEGLMTYDG
25 NTGLLATKSDETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSRDDDDVTITNLSSVEASYTVVQDQVRNSYQL
CNNGTLRVMYANGMGISFHSSEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLVRHGRNLLSIDYDRNIR
TEKIYDDHRKFTRLRIIYDQVGRPFLWLPSSGLAAVNVSYFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKWSYSYLDKSMV
LLLQSQRQYIFEDSSDRLLAVTMPSVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRIKTSFLGTGRQVFYKYGLSKL
SEIVYDSTAVTFGYDETTGVLKMNVLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPV
30 DLYRYDEISGKVEHFGKFGVYYDINQIITAVMTLSKHFDTGHRIKEVQYEMFRSLMYWMTVQYDSMGRVIRELKLGPYANTTK
YTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLL
TRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYDLOQHLFAMESSSGEEYYVASDNT
GTPLAVFSINGLMIKQLQYTAGYEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLY
MFKSNNPLSSELDLKNYVTDVKSWMFQFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNAFMALEGQV
35 ITKKLHASIREKAGHWFATTPIIIGKGIIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVKIGSADGD
LVTLTGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFYQSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKAR
DGREGSRLWTEGEKQQLLSTGRVQGYEGYVLPVEQYPELADSSSNIQFLRQNMGRK

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In a BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Mus musculus* odd Oz/ten-m homolog 2. It has 634 of 685 bases (92%) identical to bases 614-1298, 365 of 406 bases (89%) identical to bases 1420-1825, and 93 of 103 bases (90%) identical to bases 1823-1925 of *Mus musculus* odd Oz/ten-m homolog 2 (GenBank Acc: NM_011856.2) (Table 3J).

Table 3J. BLASTN of FCTR3a against *Mus musculus* odd Oz/ten-m homolog 2 (SEQ ID NO:62)

```

45 >GI|7657414|REF|NM_011856.2| MUS MUSCULUS ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA) (ODZ2),
    MRNA
        LENGTH = 8797
        SCORE = 954 BITS (481), EXPECT = 0.0
        IDENTITIES = 634/685 (92%)
        STRAND = PLUS / PLUS
        QUERY: 114 GGTCTGTCCTCCATTCCACCTACATCCTCGCTAGTCTCTCTCCCATCTGCTCAGCTGCCTAGC 173
                    |||||
55 SBJCT: 614 GGTCTGTCCTCCATTCCACCTACATCCTCGCTAGTCTCTCTCCCATCTGCTCAGCTGCCTAGC 673

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SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779

QUERY: 1157 TGGAAAAGA...GAGATGGTTTCCTTCAATACTGTGTCTAGAT...02

SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGAT 1825

SCORE = 125 BITS (63), EXPECT = 7E-26
IDENTITIES = 93/103 (90%)
STRAND = PLUS / PLUS

QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAACGTCCATGGGAATGGTGAATGTGTGTCCGGGGTG 1317

SBJCT: 1823 GATTCAGTGCAGGACTGTCCACGGAACGTGCACGGGAACGGTGAATGCGTGTCTGGACTG 1882

QUERY: 1318 TGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCTAAAG 1360

SBJCT: 1883 TGTCACTGTTTCCCAGGATTCCTAGGTGCAGACTGTGCTAAAG 1925

In another BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Gallus gallus* mRNA for teneurin-2. It has 541 of 629 bases (86%) identical to bases 502-1130, 302 of 367 bases (82%) identical to bases 1330-1696, and 87 of 103 bases (84%) identical to bases 1711-1813 of *Gallus gallus* mRNA for teneurin-2 (EMBL Acc: AJ245711.1) (Table 3K).

Table 3K. BLASTN of FCTR3a against *Gallus gallus* mRNA for teneurin-2 (SEQ ID NO:63)

>GI|6010048|EMB|AJ245711.1|GGA245711 GALLUS GALLUS MRNA FOR TENEURIN-2, SHORT SPLICE VARIANT (TEN2 GENE)
LENGTH = 2496

SCORE = 549 BITS (277), EXPECT = E-153
IDENTITIES = 541/629 (86%)
STRAND = PLUS / PLUS

QUERY: 114 GGTCTGTCCTCCATTCCACCTACATCCTCGCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173

SBJCT: 502 GGTCTGTCCTCCATTCCACCTACATCCTCGTCTAGCCTTCTCCCATCTGCTCAGCTGCCAGT 561

QUERY: 174 TCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233

SBJCT: 562 TCTCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCAT 621

QUERY: 234 CAAATCATGGACACCAACCCTGATGAGGAATTCTCCCCAATTACATACCTGCTCAGAGCA 293

SBJCT: 622 CAAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTACATACCTACTAAGAGCA 681

QUERY: 294 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353

SBJCT: 682 TGTTCAGGGCCACAGCAGGCATCCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACG 741

QUERY: 354 CTGAGGCCCCCTCTCCACCCCCCTCACAACCACACGCTGTCCCATCACCCTCGTCCGCC 413

SBJCT: 742 CTGAGGCCACCTCTCCCCCTCCTCACAACCCTCGCTGTCCCATCATCACTCGTCTGCC 801

QUERY: 414 AACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473

SBJCT: 802 AACTCCCTCAACAGGAACTCGCTCACCAACCGCCGCAACCAGATCCACGCGCCTGCTCCC 861

QUERY: 474 GCGCCCAATGACCTGGCCACCACACAGAGTCCGTTTCACTTCAGGACAGCTGGGTGCTA 533

SBJCT: 862 GCTCCCAATGACCTGGCGACCACGCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTC 921

6322, and 176 of 176 bases (100%) identical to bases 6385-6560 of *Homo sapiens* mRNA for KIAA1127 protein (GenBank Acc: AB032953) (Table 3L).

Table 3L. BLASTN of FCTR3b, c, d, and e against *Homo sapiens* KIAA1127 mRNA (SEQ ID NO:64)

```
5  >GI|6329762|DBJ|AB032953.1|AB032953 HOMO SAPIENS MRNA FOR KIAA1127 PROTEIN, PARTIAL
    CDS
      LENGTH = 6560

    SCORE = 1.097E+04 BITS (5534), EXPECT = 0.0
    IDENTITIES = 5537/5538 (99%)
    STRAND = PLUS / PLUS

    QUERY: 3267 CACCTTCTTTAGTGCTGCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 3326
    SBJCT: 1 CACCTTCTTTAGTGCTGCCCTGGGCAGAATCCCATCGTGCCTGAGACCCAGGTTCTTCA 60

    QUERY: 3327 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAAGTGC 3386
    SBJCT: 61 TGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTCTAGAAGTGC 120

    QUERY: 3387 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCTGAACCTCAT 3446
    SBJCT: 121 AGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCTGAACCTCAT 180

    QUERY: 3447 TAGGGTTACCTGATGGTGGCTGTGCGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTC 3506
    SBJCT: 181 TAGGGTTACCTGATGGTGGCTGTGCGAGGGGCATCTCTCCAGAAGTCATTCCAGGCTTC 240

    QUERY: 3507 TCCCAACCTGGCCTCCACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 3566
    SBJCT: 241 TCCCAACCTGGCCTACACCTTCATCTGGGACAAGACAGATGCGTATGGCCAAAGGGTGTA 300

    QUERY: 3567 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCAGTCTAAT 3626
    SBJCT: 301 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCAGTCTAAT 360

    QUERY: 3627 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTTCGAGCTGGACCCCTCCAACCTCGG 3686
    SBJCT: 361 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTTCGAGCTGGACCCCTCCAACCTCGG 420

    QUERY: 3687 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 3746
    SBJCT: 421 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 480

    QUERY: 3747 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 3806
    SBJCT: 481 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 540

    QUERY: 3807 TGGTCGCCGCCGGAGCATTTCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 3866
    SBJCT: 541 TGGTCGCCGCCGGAGCATTTCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 600

    QUERY: 3867 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 3926
    SBJCT: 601 GCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 660

    QUERY: 3927 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAA 3986
    SBJCT: 661 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAA 720

    QUERY: 3987 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 4046
    SBJCT: 721 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 780

    QUERY: 4047 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 4106
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SBJCT: 781 CGGCTCGCTGTGTCCGACACCAACAGCAGGAGAATCTACCGAAGTCTCTGAG 840

QUERY: 4107 TGGAAACCAAAGACCTGGCTGGGAATTTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 4166

SBJCT: 841 TGGAAACCAAAGACCTGGCTGGGAATTTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 900

QUERY: 4167 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 4226

SBJCT: 901 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 960

QUERY: 4227 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTTCGATGCCACCATGAT 4286

SBJCT: 961 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTTCGATGCCACCATGAT 1020

QUERY: 4287 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 4346

SBJCT: 1021 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 1080

QUERY: 4347 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTTCGTCTGGAGTGGCC 4406

SBJCT: 1081 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTTCGTCTGGAGTGGCC 1140

QUERY: 4407 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 4466

SBJCT: 1141 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCAT 1200

QUERY: 4467 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTCGCGGACGCCCCATGCACTGCCA 4526

SBJCT: 1201 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTCGCGGACGCCCCATGCACTGCCA 1260

QUERY: 4527 AGTTCCTGGCATTGACTACTCACTCAGCAAAGTACGATTCATCTGCCCCTGGAGTCAGC 4586

SBJCT: 1261 AGTTCCTGGCATTGACTACTCACTCAGCAAAGTACGATTCATCTGCCCCTGGAGTCAGC 1320

QUERY: 4587 CAGTGCCATTGCCATTTCTCAGCTGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 4646

SBJCT: 1321 CAGTGCCATTGCCATTTCTCAGCTGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 1380

QUERY: 4647 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 4706

SBJCT: 1381 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 1440

QUERY: 4707 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTAGGAGATGATGCCTA 4766

SBJCT: 1441 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTAGGAGATGATGCCTA 1500

QUERY: 4767 CGCGACTGATGCCATCTTGAATTCCTCATCCTTAGCTGTAGCTCCAGATGGTACCAT 4826

SBJCT: 1501 CGCGACTGATGCCATCTTGAATTCCTCATCCTTAGCTGTAGCTCCAGATGGTACCAT 1560

QUERY: 4827 TTACATTGCAGACCTTGGAATATTCCGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 4886

SBJCT: 1561 TTACATTGCAGACCTTGGAATATTCCGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 1620

QUERY: 4887 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGAGAGCAGGAGTTATATGTTTTCAA 4946

SBJCT: 1621 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCCGAGAGCAGGAGTTATATGTTTTCAA 1680

QUERY: 4947 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 5006

SBJCT: 1681 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 1740

QUERY: 5007 CACATATAGTACTGACAAATGATGTCAATTGATTGACAATAATGGGAATTCCTGAA 5066

SBJCT: 1741 CACATATAGTACTGACAAATGATGTCAATTGATTGACAATAATGGGAATTCCTGAA 1800

QUERY: 5067 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 5126

SBJCT: 1801 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 1860

QUERY:	5127	CACCCCTCAO	GGGCACCAATGGAGGCCCTCAAAGTCGTGTCCAC	AACCTGGAGCT	5186
SBJCT:	1861	CACCCTCACCGTGGGCACCAATGGAGGCCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT			1920
QUERY:	5187	TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG			5246
SBJCT:	1921	TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG			1980
QUERY:	5247	ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTGACGCGCCCCAC			5306
SBJCT:	1981	ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTGACGCGCCCCAC			2040
QUERY:	5307	GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA			5366
SBJCT:	2041	GGGGGTGGTAACCAGTCTGCACCGGGAAATGGAGAAATCTATTACCATTGACATTGAGAA			2100
QUERY:	5367	CTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTA			5426
SBJCT:	2101	CTCCAACCGTGATGATGACGTCACTGTCATCACCAACCTCTCTTCAGTAGAGGCCTCCTA			2160
QUERY:	5427	CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG			5486
SBJCT:	2161	CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG			2220
QUERY:	5487	GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCTAGCGGG			5546
SBJCT:	2221	GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCTAGCGGG			2280
QUERY:	5547	CACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA			5606
SBJCT:	2281	CACCATCACCCCCACCATTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAA			2340
QUERY:	5607	CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG			5666
SBJCT:	2341	CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG			2400
QUERY:	5667	GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCATTGACTATGATCGAAATATTCCGAC			5726
SBJCT:	2401	GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCATTGACTATGATCGAAATATTCCGAC			2460
QUERY:	5727	TGAAAAGATCTATGATGACCACCGGAAGTTACCCTGAGGATCATTTATGACCAGGTGGG			5786
SBJCT:	2461	TGAAAAGATCTATGATGACCACCGGAAGTTACCCTGAGGATCATTTATGACCAGGTGGG			2520
QUERY:	5787	CCGCCCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT			5846
SBJCT:	2521	CCGCCCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT			2580
QUERY:	5847	CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA			5906
SBJCT:	2581	CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA			2640
QUERY:	5907	GCAAGGCCGCATCGTGTCCCGCATGTTGCTGACGGGAAAGTGTGGAGCTACTCCTACCT			5966
SBJCT:	2641	GCAAGGCCGCATCGTGTCCCGCATGTTGCTGACGGGAAAGTGTGGAGCTACTCCTACCT			2700
QUERY:	5967	TGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC			6026
SBJCT:	2701	TGACAAGTCCATGGTCCTCCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC			2760
QUERY:	6027	CTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTCCACACA			6086
SBJCT:	2761	CTCTGACCGCCTCCTTGCCGTCACCATGCCCAGCGTGGCCCGGCACAGCATGTCCACACA			2820
QUERY:	6087	CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT			6146
SBJCT:	2821	CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCCTGAAAGCAATGCTTCGGTCAT			2880
QUERY:	6147	CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA			6200

SBJCT: 2881 CTTTGACTATGATGACGGCCGCATCCTGAAGACCTCCTTTTACCGGACGCCA 2940

5 QUERY: 6207 GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 6266

SBJCT: 2941 GGTGTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 3000

10 QUERY: 6267 CGTCACCTTCGGGTATGACGAGACCCTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 6326

SBJCT: 3001 CGTCACCTTCGGGTATGACGAGACCCTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 3060

15 QUERY: 6327 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 6386

SBJCT: 3061 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 3120

20 QUERY: 6387 CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 6446

SBJCT: 3121 CAGGTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 3180

25 QUERY: 6447 CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTGACCTCTA 6506

SBJCT: 3181 CTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTGACCTCTA 3240

30 QUERY: 6507 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 6566

SBJCT: 3241 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 3300

35 QUERY: 6567 TGACATCAACCAGATCATCACCCTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 6626

SBJCT: 3301 TGACATCAACCAGATCATCACCCTGCCGTGATGACCCTCAGCAAACACTTCGACACCCA 3360

40 QUERY: 6627 TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 6686

SBJCT: 3361 TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT 3420

45 QUERY: 6687 GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAACTGGGGCCCTATGCCAA 6746

SBJCT: 3421 GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAACTGGGGCCCTATGCCAA 3480

50 QUERY: 6747 TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 6806

SBJCT: 3481 TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA 3540

55 QUERY: 6807 TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 6866

SBJCT: 3541 TGACCGCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC 3600

60 QUERY: 6867 AGGCAACAGTGTGCGCCTCATGCCCTTGGCTATGACCTCCGGGATCGGATAACCAGACT 6926

SBJCT: 3601 AGGCAACAGTGTGCGCCTCATGCCCTTGGCTATGACCTCCGGGATCGGATAACCAGACT 3660

65 QUERY: 6927 CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 6986

SBJCT: 3661 CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT 3720

70 QUERY: 6987 CTTTGAATACAATTCCAAGGGCCTCTAACAAGAGCCTACAACAAGGCCAGCGGTGGAG 7046

SBJCT: 3721 CTTTGAATACAATTCCAAGGGCCTCTAACAAGAGCCTACAACAAGGCCAGCGGTGGAG 3780

75 QUERY: 7047 TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGGCCA 7106

SBJCT: 3781 TGTCCAGTACCGCTATGATGGCGTAGGACGGCGGGCTTCTACAAGACCAACCTGGGGCCA 3840

80 QUERY: 7107 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATACCCATGTCTACAA 7166

SBJCT: 3841 CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATACCCATGTCTACAA 3900

85 QUERY: 7167 TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 7226

90 SBJCT: 3901 TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT 3960

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 QUERY: 7227 GGAGAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACACTCCTCTGGC 7286
 |||||
 SBJCT: 3961 GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC 4020

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 QUERY: 7287 TGTGTTCAAGCATCAACGGCCTCATGATCAACAGCTGCAGTACACGGCCTATGGGGAGAT 7346
 |||||
 SBJCT: 4021 TGTGTTCAAGCATCAACGGCCTCATGATCAACAGCTGCAGTACACGGCCTATGGGGAGAT 4080

15
 QUERY: 7347 TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA 7406
 |||||
 SBJCT: 4081 TTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA 4140

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 QUERY: 7407 CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG 7466
 |||||
 SBJCT: 4141 CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG 4200

25
 QUERY: 7467 GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT 7526
 |||||
 SBJCT: 4201 GACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT 4260

30
 QUERY: 7527 GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC 7586
 |||||
 SBJCT: 4261 GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC 4320

35
 QUERY: 7587 AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT 7646
 |||||
 SBJCT: 4321 AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT 4380

40
 QUERY: 7647 CCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCCTATGAATTGTGAGAGTCAAGCAAG 7706
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 SBJCT: 4381 CCCGAGAGCCAAAATGTATTTCGTGCCTCCTCCCTATGAATTGTGAGAGTCAAGCAAG 4440

45
 QUERY: 7707 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 7766
 |||||
 SBJCT: 4441 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 4500

50
 QUERY: 7767 CATGGCTCTGGAAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 7826
 |||||
 SBJCT: 4501 CATGGCTCTGGAAGGACAGGTCACTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 4560

55
 QUERY: 7827 AGGTCACTGGTTTGCCACCACCGCCATCATTTGGCAAAGGCATCATGTTTGCCATCAA 7886
 |||||
 SBJCT: 4561 AGGTCACTGGTTTGCCACCACCGCCATCATTTGGCAAAGGCATCATGTTTGCCATCAA 4620

60
 QUERY: 7887 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 7946
 |||||
 SBJCT: 4621 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 4680

65
 QUERY: 7947 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 8006
 |||||
 SBJCT: 4681 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 4740

70
 QUERY: 8007 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 8066
 |||||
 SBJCT: 4741 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 4800

75
 QUERY: 8067 CATCGGCCGCAAGGTGCTAGAGAGCGGGTGAACTGACCGTGTCCAGCCACGCTGCT 8126
 |||||
 SBJCT: 4801 CATCGGCCGCAAGGTGCTAGAGAGCGGGTGAACTGACCGTGTCCAGCCACGCTGCT 4860

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 QUERY: 8127 GGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT 8186
 |||||
 SBJCT: 4861 GGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCCAGTACTCCACGCTGCTGCT 4920

85
 QUERY: 8187 CAGCATCCGCTATGGCCTCACCCCGACACCCTGGACGAAGAGAAGGCCGCGTCTGGA 8246
 |||||
 SBJCT: 4921 CAGCATCCGCTATGGCCTCACCCCGACACCCTGGACGAAGAGAAGGCCGCGTCTGGA 4980

90
 QUERY: 8247 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 8306

QUERY: 9295 AAAATGGTCTATAATCACTACAGATAAAATTTCACTCTTTTGTGGAGATTCCA 9354
 |||||
 SBJCT: 6029 AAAATGGTGGCTATAATCACTACAGATAAAATTTCACTCTTTTGTCTTTGGAGATTCCA 6088

 QUERY: 9355 TTGTGGACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGT 9414
 |||||
 SBJCT: 6089 TTGTGGACAGTAATACGCAGTTACAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGT 6148

 QUERY: 9415 ATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAACAGGTACCACTTCTGATC 9474
 |||||
 SBJCT: 6149 ATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAACAGGTACCACTTCTGATC 6208

 QUERY: 9475 ACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTAAAAATTATTAGTG 9534
 |||||
 SBJCT: 6209 ACCCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTAAAAATTATTAGTG 6268

 QUERY: 9535 TGTGTTGTTTGGTCCAGAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 9588
 |||||
 SBJCT: 6269 TGTGTTGTTTGGTCCAGAACTGAGACAATCACATGACAGTCACCACGAGGAGAG 6322

 SCORE = 349 BITS (176), EXPECT = 2E-92
 IDENTITIES = 176/176 (100%)
 STRAND = PLUS / PLUS

 QUERY: 9651 GTCTAATAAGAACTTTGGTACAGGAACCTTTTTGTAATATACATGTATGAATTGTTTCATC 9710
 |||||
 SBJCT: 6385 GTCTAATAAGAACTTTGGTACAGGAACCTTTTTGTAATATACATGTATGAATTGTTTCATC 6444

 QUERY: 9711 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 9770
 |||||
 SBJCT: 6445 GAGTTTTTATATTAATTTTAATTTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 6504

 QUERY: 9771 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAACTCCTGTG 9826
 |||||
 SBJCT: 6505 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAACTCCTGTG 6560

In this search it was also found that the FCTR3bcd and e nucleic acids had homology to five fragments of *Mus musculus* mRNA for Ten-m2. It has 5498 of 6108 bases (90%) identical to bases 2504-8610, 1095 of 1196 bases (91%) identical to bases 103-1298, 1000 of 1088 bases (91%) identical to bases 1420-2540, 81 of 89 bases (91%) identical to bases 8655-8743, and 30 of 32 bases (93%) identical to bases 7-38 of *Mus musculus* mRNA for Ten-m2 (Table 3M).

Table 3M. BLASTN of FCTR3b, c, d, and e against *Mus musculus* mRNA for Ten-m2 Mrna (SEQ ID NO:65)

>GI|4760777|DBJ|AB025411.1|AB025411 MUS MUSCULUS MRNA FOR TEN-M2, COMPLETE CDS
 LENGTH = 8797

 SCORE = 7263 BITS (3664), EXPECT = 0.0
 IDENTITIES = 5498/6108 (90%), GAPS = 1/6108 (0%)
 STRAND = PLUS / PLUS

 QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2637
 |||||
 SBJCT: 2504 GATGGCTGCCCTGATTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2563

 QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
 |||||
 SBJCT: 2564 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCCATGGAAACTTCC 2623

 QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
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SBJCT: 2624 TGCCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCCTCGACCCTGACTGC 2683

QUERY: 2758 TGCCTGCAGCCTGTGTCAGAACAGCCTGCTCTGCCGGGGTCCCGACCCACTGGAC 2817
|||||

SBJCT: 2684 TGCCTACAGTCAGCCTGTGTCAGAACAGCCTGCTCTGCCGGGGTCTCGGGACCCCTTGGAC 2743

QUERY: 2818 ATCATTAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877
|||||

SBJCT: 2744 ATCATTAGCAAGGTGACAGACTGGCCTGCAGTGAAGTCCTTCTATGACCGCATCAAG 2803

QUERY: 2878 CTCTTGGCAGGCAAGGATAGCACCCACATCATTCTGGAGAGAACCCTTTCAACAGCAGC 2937
|||||

SBJCT: 2804 CTCTTGGCAGGCAAGGACAGCACCCACATCATTCTGGAGACAACCCTTCAATAGCAGC 2863

QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACACAGATGGAACCTCCCTGGTGGTGTG 2997
|||||

SBJCT: 2864 CTGGTGTCTCTGATCCGAGGCCAAGTAGTAACCATGGATGGGACTCCCTTGGTGGTGTG 2923

QUERY: 2998 AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCAGC 3057
||

SBJCT: 2924 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGATGGCAGC 2983

QUERY: 3058 TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTTC 3117
||

SBJCT: 2984 TTTGACCTGATTGCCAATGGGGTTCTGCCTTGACTCTTCACTTTGAGCGAGCCCCCTTC 3043

QUERY: 3118 ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCTG 3177
|||||

SBJCT: 3044 ATGAGCCAGGAGCGCACAGTGTGGCTGCCATGGAACAGCTTCTATGCCATGGACACCCTG 3103

QUERY: 3178 GTGATGAAGACCGAGGAGAACTCCATCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237
||

SBJCT: 3104 GTAATGAAGACCGAGGAAAACCTCCATCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCA 3163

QUERY: 3238 GATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCCTGGGCAGAAT 3297
|||||

SBJCT: 3164 GATCCAATCATCATCTCCTCTCCTCTGTCCACCTTCTTCAGCGCTTCCCCTGCCTCGAAC 3223

QUERY: 3298 CCCATCGTGCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357
|||||

SBJCT: 3224 CCCATTGTGCTGAGACCCAGGTTCTTCATGAAGAAATTGAGCTCCCTGGTACCAATGTG 3283

QUERY: 3358 AAACCTCGCTATCTGAGCTCTAGAAGTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417
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SBJCT: 3284 AAGCTCCGTTATCTCAGCTCTAGAAGTGCAGGGTATAAGTCGCTGCTGAAGATCACCATG 3343

QUERY: 3418 ACCCAGTCCACAGTGCCCTGAACCTCATTAGGGTTACCTGATGGTGGCTGTGAGGGG 3477
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SBJCT: 3344 ACGCAGTCCACAGTGCCCTGAACCTCATCAGGGTTCACTTGATGGTTGCTGTAGAGGGG 3403

QUERY: 3478 CATCTCTCCAGAAGTCATTCCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537
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SBJCT: 3404 CATCTCTCCAGAAGTCATTCCAGGCTTCTCCCAACCTAGCCTACACATTCATCTGGGAC 3463

QUERY: 3538 AAGACAGATGCGTATGGCCAAAGGGTGTATGGAAGTCTCAGATGCTGTTGTGTCTGTGCGG 3597
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SBJCT: 3464 AAGACAGATGCTTATGGCCAAAGGGTTTATGGCCTATCGGATGCTGTTGTGTCTGTTGGG 3523

QUERY: 3598 TTTGAATATGAGACCTGTCCAGTCTAATTTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657
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SBJCT: 3524 TTTGAATATGAGACCTGCCCCAGTCTCATCTGTGGGAGAAAAGGACAGCCCTGCTTCAG 3583

QUERY: 3658 GGATTGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717
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SBJCT: 3584 GGATTGAGCTGGACCCCTCCAACCTTGGAGGCTGGTCCCTGGACAAACACCACACCCTC 3643

QUERY: 3718 AATGTTAAAAGTGAATCCTACACAAAGGCACTGGGGAAAACAGTTCTTGACCCAGCAG 3777
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SBJCT: 3644 AATGTGAAAAGCGGAATACTACACAAAGGACAGGGGAGAACAGTTCTTGACCCAGCAG 3703

QUERY: 3778 CCTGCCATCATCACCAGCATCATGGGCAATGGTCGCCGCCGAGCATTTCCTGTCCCAGC 3837
 SBJCT: 3704 CCTGCCATCATCAGAGCATCATGGGCAACGGTCGCCGCCAGAGCATTTCCTGTCCCAGC 3763
 5 QUERY: 3838 TGCAACGGCCTTGCTGAAGGCAACAAGCTGCTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897
 SBJCT: 3764 TGCAATGGCCTTGCTGAAGGCAACAACTGTTAGCCCCGTGGCCCTGGCTGTGGGGATC 3823
 10 QUERY: 3898 GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTCCCTCTCGAAAT 3957
 SBJCT: 3824 GATGGGAGCCTCTTGTGTTGGTGACTTCAACTATATCCGGCGCATCTTCCCTCTCGAAAT 3883
 15 QUERY: 3958 GTGACCAGCATCTTGGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017
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 SBJCT: 3944 AAGTACTACTTGGCTGTGGACCCCGTGACTGGCTCACTCTACGTCTCTGACACCAACAGT 4003
 25 QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGAACCAAAGACCTGGCTGGGAATTCGGAA 4137
 SBJCT: 4004 CGCCGAATCTACCGAGTCAAGTCTCTGAGCGGAGCCAAAGACCTGGCTGGGAATTCGGAA 4063
 30 QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197
 SBJCT: 4064 GTTGTGGCAGGGACTGGCGAACAATGTCTACCCTTTGATGAAGCCCGCTGTGGGGATGGA 4123
 35 QUERY: 4198 GGGGAAGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257
 SBJCT: 4124 GGGGAAGGCTGTGGACGCCACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4183
 40 QUERY: 4258 CTCATGTACTTTGTTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317
 SBJCT: 4184 CTTATGTACTTTGTTGATGCCACCATGATCCGGAAGGTTGACCAAAACGGAATCATCTCC 4243
 45 QUERY: 4318 ACCCTGTGGGCTCCAATGACCTCACTGCCGTCCGGCCGCTGAGCTGTGATTCCAGCATG 4377
 SBJCT: 4244 ACCCTGTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCGAGCATG 4303
 50 QUERY: 4378 GATGTAGCCCAGGTTCTGCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC 4437
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 55 QUERY: 4438 TCCTTGTATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497
 SBJCT: 4364 TCCCTGTACGTTCTGGAGAACAACGTATCCTGCGGATCACGGAGAACCACCAGGTCAGC 4423
 60 QUERY: 4498 ATCATTCGCGGACGCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAA 4557
 SBJCT: 4424 ATCATTCGCGGACGGCCTATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAA 4483
 65 QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617
 SBJCT: 4484 CTCGCCATCCACTCTGCGCTGGAATCAGCCAGCGCCATTGCCATTTCTCACACTGGGGTC 4543
 70 QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677
 SBJCT: 4544 CTCTACATCACTGAGACGACGAGAAGAAGATCAACCGCCTACGCCAAGTCACCACCAAT 4603
 QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737
 SBJCT: 4604 GGAGAGATCTGCCTTTAGCCGGGGCGCCTCAGACTGTGACTGCAAAAACGATGTCAAC 4663
 QUERY: 4738 TGCAACTGCTATTTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCATCA 4797
 SBJCT: 4664 TGCATCTGCTACTCGGAGATGACGCTTACGCCACGGACGCCATCCTGAACTCGCCGTCC 4723
 QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTTACATTGCAGACCTTGAAATATTTCGGATC 4857

SBJCT: 6824 TATGACCTCCGTGACCGGATAACCAGGCTAGGGGACGTGCAGTACAAATCGATGACGAT 6883
 QUERY: 6958 GGCTATCTGAGAGAGGGTCTGACATCTTGAATACAATTCCAGCCTCCTAACA 7017
 SBJCT: 6884 GGCTATTGTGCGCAGAGAGGGTCTGACATCTTGAATACAATTCCAGGCGCTTCTGACG 6943
 QUERY: 7018 AGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGG 7077
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 QUERY: 7078 CGGGCTTCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC 7137
 SBJCT: 7004 CGGGCTTCTACAAGACCAACCTGGGCCACCACCTACAGTACTTCTACTCCGACCTCCAC 7063
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 SBJCT: 7244 CAACTGCAGTACACAGCCTATGGGGAGATCTACTATGACTCCAATCCAGACTTCCAGATG 7303
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 SBJCT: 7304 GTCATTGGCTTCCACGAGGCGCTCTATGACCCCTCACCAAGCTCGTCCACTTTACTCAA 7363
 QUERY: 7438 CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497
 SBJCT: 7364 CGTGATTATGACGTGCTGGCAGGACGCTGGACGTCCCCGACTACACCATGTGGAGGAAC 7423
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 SBJCT: 7424 GTGGGCAAGGAGCCAGCCCCCTTCAACCTGTACATGTTCAAGAACAACAATCCTCTGAGC 7483
 QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGA 7617
 SBJCT: 7484 AATGAGCTGGACTTAAAGAACTACGTGACAGACGTGAAGAGCTGGCTTGTGATGTTTGA 7543
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 SBJCT: 7544 TTTCACTCAGCAACATCATTCCTGGATTCCTGAGAGCCAAAATGTATTTGTGCTCCTCC 7603
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 SBJCT: 7604 CCCTATGAATGTGAGAGTCAAGCAAGCGAGAACGGACAGCTCATTACAGGTGTCCAG 7663
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 SBJCT: 7664 CAGACAACAGAGAGACATAACCAGGCCTTCCTGGCTCTGGAAGGACAGGTCACTACTAAA 7723
 QUERY: 7798 AAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC 7857
 SBJCT: 7724 AAGCTCCATGCCAGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACCACCACACCATC 7783
 QUERY: 7858 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGCGTGTCCAGC 7917
 SBJCT: 7784 ATCGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACAGGAGTGTCTAGC 7843
 QUERY: 7918 ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGAC 7977
 SBJCT: 7844 ATCGCCAGTGAGGACAGCCGCAAGGTAGCATCCGTGTTGAACAATGCCTACTACTTAGAC 7903

QUERY: 1524 GGTAACACAAGAAGTCCCACCAGGGGTGTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583
 SBJCT: 1480 GGTGACACAGTCCCACCAGGGGTGTTTGGAGGTCACATCAGTCAGCC 1539
 5 QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTGGTGTTCACATAAG 1643
 SBJCT: 1540 TCAATTCCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTTCGGTGTCTATATAAG 1599
 10 QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703
 SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659
 15 QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGAGCATACAGACCTTGGTTTCAGAA 1763
 SBJCT: 1660 GAAATGGAGCGTGGTCGAGTCGCCCAGGGAACGCCGAGCATCCAGACTCTGGTGCAGAA 1719
 20 QUERY: 1764 TGAAGCCGTGTTTGTGTCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
 SBJCT: 1720 CGAGGCTGTGTTTGTGTCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779
 25 QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCTTAGATTAGTGCAGGACTG 1883
 SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGATTAGTGCAGGACTG 1839
 30 QUERY: 1884 TCCACGTAAGTCCATGGGAATGGTGAATGTGTGTCCGGGTGTGTCACTGTTTCCCAGG 1943
 SBJCT: 1840 TCCACGGAAGTGTACGGAACGGTGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1899
 35 QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 2003
 SBJCT: 1900 ATTCTAGGTGCAGACTGTGCTAAAGCTGCCTGCCCTGTACTGTGCAGCGGAAATGGACA 1959
 40 QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCAGCTGCC 2063
 SBJCT: 1960 GTATTCTAAAGGAACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGTGATGTGCC 2019
 45 QUERY: 2064 CATGAATCAGTGCATCGATCCTTCTGCGGGGGCCACGGCTCCTGCATTGATGGGAAGT 2123
 SBJCT: 2020 TATGAACCAATGTATCGATCCTTCTGTGGGGGCCATGGCTCCTGCATTGATGGGAAGT 2079
 50 QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCAC 2183
 SBJCT: 2080 CGTGTGTGCTGCTGGCTACAAGGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCTAC 2139
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 60 QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGCAGTGGGCATGGGCACGTA 2303
 SBJCT: 2200 TCTCAACTGTGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGTAGTGGGCATGGCACTTA 2259
 65 QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
 SBJCT: 2260 CCTCCCTGACTCCGGCCTCTGCAGCTGTGATCCGAAGTGGATGGGTCCCGACTGCTCTGT 2319
 70 QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423
 SBJCT: 2320 T--GTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2376
 QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2483
 SBJCT: 2377 TGAAGAGGGCTGGACAGGCGCAGCTTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2436
 QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
 SBJCT: 2437 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2496
 QUERY: 2544 CACCATTG 2551
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5 SBJCT: 3967 AAGTACTACGCTGTGGACCCTGTGACTGGCTCGCTCTATGTCACACCAACAGT 4026

QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAACCAAGACCTGGCTGGGAATTCGGAA 4137

SBJCT: 4027 CGCCGGATCTACCGAGTCAAGTCTCTAAGCGGAGCCAAAGACCTGGCTGGGAATTCGGAA 4086

10 QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197

SBJCT: 4087 GTTGTGGCCGGGACTGGCGAACAATGTCTACCCTTTGATGAAGCCCGCTGTGGGGATGGC 4146

15 QUERY: 4198 GGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257

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SBJCT: 4267 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCTAGCATG 4326

30 QUERY: 4378 GATGTAGCCAGGTTTCGTCTGGAGTGGCCAAACAGACCTTGCTGTCAATCCCATGGATAAC 4437

SBJCT: 4327 GACGTGGCCAGGTCGCTCTAGAATGGCCGACAGACCTTGCGGTCAACCCCATGGACAAT 4386

35 QUERY: 4438 TCCTTGATGTTCTAGAGAACAAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497

SBJCT: 4387 TCCCTGTACGTCCTGGAGAACAAACGTCATCCTGCGGATCACCGAGAATCACCAGGTCAGC 4446

40 QUERY: 4498 ATCATTCGCGGACGCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAA 4557

SBJCT: 4447 ATCATCGCGGACGGCCCATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAG 4506

45 QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617

SBJCT: 4507 CTCGCCATCCACTCTGCTCTGGAGTCAGCCAGCGCCATCGCCATTTCTCACACCGGGGTG 4566

50 QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677

SBJCT: 4567 CTCTACATCACCGAGACGGACGAGAAGAAGATCAACCGCTACGCCAGGTCACCACCAAC 4626

55 QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737

SBJCT: 4627 GGAGAGATCTGCCTTTAGCCGGGGCAGCCTCAGACTGTGACTGCAAAAATGACGTCAAC 4686

60 QUERY: 4738 TGCAACTGCTATTCAGGAGATGATGCCTACGCGACTGATGCCATCTTGAATTCCCCATCA 4797

SBJCT: 4687 TGCATCTGCTATTCGGGAGATGACGCATACGCCACGGATGCCATCTTGAATCCCCGTCC 4746

65 QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAATATTCCGATC 4857

SBJCT: 4747 TCCTTAGCTGTGGCTCCGGATGGCACCATCTACATCGCAGACCTCGGAATATCCGGATC 4806

70 QUERY: 4858 AGGGCGGTGAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917

SBJCT: 4807 AGGGCGGTGAGCAAAAACAACCTGTTCTTAACGCGTTCAACCAGTATGAGGCTGCGTCT 4866

QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977

SBJCT: 4867 CCGGGAGAACAGGAACGTACGTGTTCAACGCCGATGGTATCCATCAGTACACCGTGAGC 4926

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SBJCT: 4927 CTGGTGACCGGGGAGTACTTATACAATTTACCTACAGCGCTGACAATGATGTACCGAG 4986

QUERY: 5038 TTGATTGACAATAATGGGAATTCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGT 5097

SBJCT: 4987 TTGATTGACAACAACGGGAATTCCTAAAGATCCGCCGGGACAGCAGTGGCATGCCCCGA 5046

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QUERY: 5098 CACCTGCTCCTGACAACCAGATCATCACCTCACCGTGGGATGGAGGCCTC 5157
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SBJCT: 5047 CACCTGCTCATGCCTGATAATCAGATCATCACCTTACGGTGGGCACCAACGGAGGCCTC 5106

QUERY: 5158 AAAGTCGTGTCCACACAGAACCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 5217
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SBJCT: 5107 AAAGCCGTGTCAACGCAGAACCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA 5166

QUERY: 5218 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA 5277
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SBJCT: 5167 CTCCTAGCCACCAAGAGCGATGAAACCGGATGGACAACCTTTTATGACTATGACCACGAG 5226

QUERY: 5278 GGCCGCCTGACCAACGTGACGCGCCCCACGGGGTGGTAACAGTCTGCACCGGGAAATG 5337
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SBJCT: 5227 GGCCGTCTGACCAATGTGACTCGCCCCACGGGGTGGTGACCAGCCTGCACCGGGAAATG 5286

QUERY: 5338 GAGAAATCTATTACCATTTGACATTGAGAACTCCAACCGTGATGATGACGTCACTGTCTATC 5397
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QUERY: 5398 ACCAACCTCTCTTCAGTAGAGGCCTCCTACACAGTGGTACAAGATCAAGTTCGGAACAGC 5457
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SBJCT: 5347 ACCAACCTCTCTTCAGTGGAGGCCTCCTACACCGTGGTACAAGATCAAGTGCAGAACAGC 5406

QUERY: 5458 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC 5517
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SBJCT: 5407 TACCAGCTCTGCAGCAACGGGACCTGCGCGTCATGTACGCCAACGGCATGGGCGTCAGC 5466

QUERY: 5518 TTCCACAGCGAGCCCCATGTCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC 5577
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SBJCT: 5467 TTCCACAGCGAGCCCCACGTCTCGCAGGCACCCTCACCCCCACCATCGGGCGCTGTAAC 5526

QUERY: 5578 ATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG 5637
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SBJCT: 5527 ATCTCCCTGCCCATGGAGAACGGCCTGAACTCCATCGAGTGGCGCCTGAGGAAGGAACAG 5586

QUERY: 5638 ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG 5697
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SBJCT: 5587 ATTAAAGGCAAAGTCACCATCTTTGGGAGGAAGCTTCGGGTCCACGGAAGGAACCTCTG 5646

QUERY: 5698 TCCATTGACTATGATCGAAATATTCGGACTGAAAAGATCTATGATGACCACCGGAAGTTC 5757
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SBJCT: 5647 TCCATTGATTATGACCAGAAATATCCGCACTGAGAAGATCTATGACGACCACCGGAAGTTC 5706

QUERY: 5758 ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCTCTGGCTGCCAGCAGCGGG 5817
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SBJCT: 5707 ACCCTGAGGATCATTTATGACCAGGTGGGCCGCCCTTCTGTGGCTCCCCAGCAGTGA 5766

QUERY: 5818 CTGGCAGCTGTCAACGTGTCATACTTCTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGG 5877
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SBJCT: 5767 CTGGCGGCCGTCAATGTCTCCTACTTCTTCAACGGGCGCCTGGCCGGCTCCAGCGCGGG 5826

QUERY: 5878 GCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGCATCGTGTCCCGCATGTTTCGCT 5937
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SBJCT: 5827 GCCATGAGCGAGAGGACAGACATTGACAAGCAAGGCCGGATTGTGTCCCGAATGTTTCGCC 5886

QUERY: 5938 GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCCTCCTGCTTCAGAGC 5997
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SBJCT: 5887 GACGGGAAAGTCTGGAGCTATTCTACCTTGACAAGTCCATGGTCCTCCTGCTGCAGAGC 5946

QUERY: 5998 CAACGTGAGTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTACCATGCCC 6057
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SBJCT: 5947 CAGCGTCAGTACATATTTGAATATGACTCCTCTGACCGCCTCCACGCAGTACCATGCCC 6006

QUERY: 6058 AGCGTGGCCCGGCACAGCATGTCCACACACCTCCATCGGCTACATCCGTAATATTTAC 6117
          |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
SBJCT: 6007 AGTGTGCCCCGGCACAGCATGTCCACGCACACCTCCATTGGCTACATCCGGAACATTTAC 6066

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 QUERY: 6118 AACCCGCCTTACGAATGCTTCGGTCATCTTTGACTACAGTGATGCCGCATCCTG 6177
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 SBJCT: 6067 AACCCACCGGAAAGCAACGCCTCGGTTCATCTTTGACTACAGTGATGACGGCCGCATCCTG 6126

10
 QUERY: 6178 AAGACCTCCTTTTGGGACCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAG 6237
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 SBJCT: 6127 AAGACGTCTTCTCGGACCGGGCGCCAGGTGTTCTATAAGTACGGAAACTGTCCAAG 6186

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 QUERY: 6238 TTATCAGAGATTGTCTACGACAGTACCGCGTCACCTTCGGGTATGACGAGACCACTGGT 6297
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 SBJCT: 6187 TTATCGGAGATCGTCTACGACAGCACTGCCGTACCTTCGGCTATGACGAGACCACTGGC 6246

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 QUERY: 6298 GTCTTGAAGATGGTCAACCTCCAAAGTGGGGCTTCTCCTGCACCATCAGGTACCGGAAG 6357
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 SBJCT: 6247 GTCCTGAAGATGGTGAATCTCCAAAGCGGGGCTTCTCCTGTACCATCAGGTACCGAAAG 6306

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 QUERY: 6358 ATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC 6417
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 QUERY: 6418 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA 6477
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 SBJCT: 6367 AGGTTCGATTACACCTACCACGACAACAGCTTCCGCATCGCCAGCATCAAGCCCGTCATC 6426

35
 QUERY: 6478 AGTGAGACTCCCCTCCCCGTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA 6537
 |||||
 SBJCT: 6427 AGTGAGACTCCCCTTCCCGTTGACCTCTACCGCTACGATGAGATTTCTGGCAAGGTGGAA 6486

40
 QUERY: 6538 CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCCTGCCGTG 6597
 |||||
 SBJCT: 6487 CACTTCGGCAAGTTTCGGGGTCATCTACTACGACATCAACCAGATCATCACCCTGCCGTC 6546

45
 QUERY: 6598 ATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG 6657
 |||||
 SBJCT: 6547 ATGACACTCAGCAAGCACTTTGACACCCATGGGCGCATCAAGGAAGTGCAGTATGAGATG 6606

50
 QUERY: 6658 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG 6717
 |||||
 SBJCT: 6607 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGTATGGGCAGGGTGATCAAG 6666

55
 QUERY: 6718 AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG 6777
 |||||
 SBJCT: 6667 AGGGAAGTGAAGTGGGGCCCTATGCCAACACCACAAAGTACACCTATGACTACGACGGG 6726

60
 QUERY: 6778 GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCGACCTGGCGCTACAGCTATGAC 6837
 |||||
 SBJCT: 6727 GACGGCCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGTTATAGCTATGAC 6786

65
 QUERY: 6838 CTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC 6897
 |||||
 SBJCT: 6787 CTCAATGGGAACCTGCACCTGCTAAACCCAGGAAACAGTGCTGCGCCTCATGCCGTTACGC 6846

70
 QUERY: 6898 TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGAT 6957
 |||||
 SBJCT: 6847 TATGACCTCCGTGACCGGATAACCAGGCTAGGGGACGTGCAGTACAAAATCGATGATGAT 6906

75
 QUERY: 6958 GGCTATCTGTGCCAGAGAGGGTCTGACATCTTCGAATACAATTCCAAGGGCCTCCTAACA 7017
 |||||
 SBJCT: 6907 GGCTATTATATGCCAGAGAGGATCTGACATCTTTGAATACAACCTCCAAGGGCCTTCTAACG 6966

80
 QUERY: 7018 AGAGCCTACAACAAGGCCAGCGGTGGAGTGTCCAGTACCGCTATGATGGCGTAGGACGG 7077
 |||||
 SBJCT: 6967 AGAGCGTACAACAAGGCCAGCGGTGGAGTGTGCAGTACCGCTATGATGGCGTGAGCCGC 7026

85
 QUERY: 7078 CGGGCTTCTTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC 7137
 |||||
 SBJCT: 7027 CGGGCTTCTTACAAGACCAACCTGGGCCACCACCTACAGTACTTCTATTCCGACCTCCAC 7086

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QUERY: 7138 AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTAC 7197
|||
SBJCT: 7087 CACCCACAATCACCCATGTTTACAACCACTCCAACCTCTGAGTACCTCACTCTAC 7146

5 QUERY: 7198 TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT 7257
||
SBJCT: 7147 TATGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGTAGTGGGGAAGAGTACTATGTT 7206

10 QUERY: 7258 GCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTTACGATCAACGGCCTCATGATCAAA 7317
|||
SBJCT: 7207 GCCTCAGATAACACCGGGACTCCTCTGGCTGTGTTTTAGTATCAATGGCCTCATGATCAAG 7266

15 QUERY: 7318 CAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCGACTTCCAGATG 7377
||
SBJCT: 7267 CAACTCCAATACACAGCCTATGGGGAGATTTACTATGACTCCAATCCAGACTTTTACAGATG 7326

20 QUERY: 7378 GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAG 7437
|||
SBJCT: 7327 GTCATCGGCTTCCACGGAGGCCTCTACGACCCCTCACCAAGCTCGTTCACCTTTACGCAG 7386

25 QUERY: 7438 CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497
|||
SBJCT: 7387 CGTGATTATGACGTGTGGCAGGACGGTGGACGTCCCCGACTACACCATGTGGAGGAAT 7446

30 QUERY: 7498 GTGGGCAAGGAGCCGGCCCCCTTTAACCTGTATATGTTCAAGAGCAACAATCCTCTCAGC 7557
|||
SBJCT: 7447 GTGGGCAAGGAGCCAGCCCCCTTCAACCTGTACATGTTCAAGAACAACAATCCACTCAGT 7506

35 QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGA 7617
|||
SBJCT: 7507 AATGAGCTGGATTTAAAGAACTACGTGACAGACGTGAAGAGCTGGCTCGTGATGTTTGA 7566

40 QUERY: 7618 TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTTCGTGCCTCCT 7677
|||
SBJCT: 7567 TTTCAGCTCAGCAACATCATTCCTGGATTCCCAAGAGCCAAAATGTATTTGTGCCTCCC 7626

45 QUERY: 7678 CCCTATGAATTGTGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA 7737
|||
SBJCT: 7627 CCCTATGAAGTGTGAGAGCCAAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAG 7686

50 QUERY: 7738 CAGACAACAGAGAGACATAACCAGGCCTTCATGGCTCTGGAAGGACAGGTCACTACTAAA 7797
|||
SBJCT: 7687 CAGACAACAGAGAGGCATAACCAGGCCTTCTGGCTCTAGAAGGACAGGTCACTCTCTAAA 7746

55 QUERY: 7798 AAGCTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC 7857
|||
SBJCT: 7747 AAGCTCCATGCAGGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACGACCACGCCCATC 7806

60 QUERY: 7858 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC 7917
|||
SBJCT: 7807 ATCGGCAAAGGCATCATGTTTCGCCATCAAAGAAGGGCGGGTGACCACAGGCGTGTCTAGC 7866

65 QUERY: 7918 ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGAC 7977
|||
SBJCT: 7867 ATCGCCAGTGAGGACAGCCGCAAGGTAGCATCCGTGTTGAACAACGCCTACTACTTGGAC 7926

70 QUERY: 7978 AAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCC 8037
|||
SBJCT: 7927 AAGATGCACTACAGCATCGAGGGCAAGGACACACACTACTTCGTGAAGATCGGTGCAGCG 7986

QUERY: 8038 GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGTG 8097
|||
SBJCT: 7987 GACGGTGACCTGGTTACGCTGGGGACCACCATTGGGCGCAAGGTGCTGGAGAGCGGGTG 8046

QUERY: 8098 AACGTGACCGTGTCCCAGCCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAAC 8157
|||
SBJCT: 8047 AACGTGACCGTGTACAGCCCACGCTGCTGGTGAACGGCAGGACTCGAAGGTTACCAAC 8106

QUERY: 8158 ATTGAGTTCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTACCCCCGACACC 8217
|||

QUERY: 690 ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAAACTCGGCCCTTACCTGACTGACTC 749
 SBJCT: 543 ATCGAGGCCCTCTGGCTTGTCCAGCCGCGAGAAGTCTAGCCCTTCTGACTGATTTC 602
 5 QUERY: 750 TGACAACGAAAAACAATCAGATGATGAGAACGGTCGTCCCATTCACCTACATCCTCGCC 809
 SBJCT: 603 TGACAATGAAAAATAAATCGGATGACGACAATGGTCGACCCATTCCACCTACATCCTCGTC 662
 10 QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATTAATCCTCCACCAGTTAGCTGCCA 869
 SBJCT: 663 TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATTAATCCTCCACCAGTTAGCTGCCA 722
 15 QUERY: 870 GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCTGATGAGGA 929
 SBJCT: 723 GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCAACCCCGATGAGGA 782
 20 QUERY: 930 ATTCTCCCCAATTACACTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
 SBJCT: 783 ATTCTCCCCAATTACACTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGTAG 842
 25 QUERY: 990 TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCACCCCTCACAA 1049
 SBJCT: 843 TGGCCCTCCGAACCACCACAGCCAGTCAACGCTGAGGCCCCCTCTGCCACCTCCTCATAA 902
 30 QUERY: 1050 CCACACGCTGTCCCATCACCCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
 SBJCT: 903 CCACACCTGTCCCATCACCCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 962
 35 QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169
 SBJCT: 963 TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCACCCAATGACCTGGCCACCACGCCGGA 1022
 40 QUERY: 1170 GTCCGTTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCAGCAGCTCTTCCCGGGGATA 1229
 SBJCT: 1023 GTCCGTTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCAGCAGCTCTTCCCGGGGATA 1082
 45 QUERY: 1230 CTTCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCAGCAGCTCTTCCCGGGGATA 1289
 SBJCT: 1083 CTTCTCTTCAAGACCTCCTCGGGGAGCACACCCTTGTTTCAGCAGCTCTTCCCGGGGATA 1142
 50 QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCCGCTGCTGCCAGGAATACTTT 1349
 SBJCT: 1143 CCCTTTGACCTCAGGAACGGTTTATACACACCAACCCCGCTGCTGCCAGGAATACTTT 1202
 55 QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCAAATACTGCAGCTGGAAATGTGCTGC 1409
 SBJCT: 1203 CTCTAGGAAGGCTTTCAAGCTGAAGAAGCCCTCAAATACTGCAGTTGGAAATGCGCCGC 1262
 60 QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTGGCTATTTTGCTGGCGTATTTTCATAG 1465
 SBJCT: 1263 CCTGTCTGCCATTGCCGCTGCCCTCCTCTGGCCATTTTGCTGGCCTATTTTCATAG 1318
 SCORE = 1427 BITS (720), EXPECT = 0.0
 IDENTITIES = 996/1088 (91%)
 STRAND = PLUS / PLUS
 65 QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
 SBJCT: 1440 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGCGGCGAGGCAGAAGTCGGTCGACG 1499
 70 QUERY: 1524 GGTAACACAAGAAGTCCACACAGGGGTGTTTGGAGGTCACAAATTCACATCAGTCAGCC 1583
 SBJCT: 1500 GGTGACACAGGAAGTCCACACAGGGGTGTTTGGAGGTCACAGATTACATCAGTCAGCC 1559
 65 QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTGGTGTTCACATAAG 1643
 SBJCT: 1560 TCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGATGCCCTCTTCGGCGTCTACATAAG 1619
 70 QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703
 SBJCT: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703

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5  SBJCT: 1620 AAGAGGACTGCCACCATCTCATGCACAGTATGACTTCATGGAACGCCTGGACGGAAAGGA 1679
    QUERY: 1704 GAAGTGGAGCGTTGAGTCTCCAGGGAACGCCGAGCATAACCTTGGTTTCAGAA 1763
    |||||
10 SBJCT: 1680 GAAGTGGAGTGTGGTCGAGTCAACCAGGGAACGCCGAGCATCCAGACCCTGGTGCAGAA 1739
    QUERY: 1764 TGAAGCCGTGTTTGTGTCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
    |||||
15 SBJCT: 1740 CGAGGCTGTGTTTCGTGTCAGTACTTGGATGTGGGCCTGTGGCACCTCGCCTTCTACAATGA 1799
    QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCTTCAATACTGTTGTCTTAGATTCACTGCAGGACTG 1883
    |||||
20 SBJCT: 1800 CGGCAAGGACAAGGAGATGGTCTCCTTCAATACGGTGTCTTAGATTCACTGCAGGACTG 1859
    QUERY: 1884 TCCACGTAAGTCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943
    |||||
25 SBJCT: 1860 TCCACGAAACTGCCACGGGAACGGCGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1919
    QUERY: 1944 ATTTCTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 2003
    |||||
30 SBJCT: 1920 ATTCCTAGGTGCAGACTGCGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 1979
    QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGCTGGAAAGGTGCAGAGTGCAGACGTGCC 2063
    |||||
35 SBJCT: 1980 GTATTCCAAAGGGACATGCCAGTGCTACAGTGGCTGGAAAGGAGCAGAATGCGATGTGCC 2039
    QUERY: 2064 CATGAATCAGTGCATCGATCCTTCTGCGGGGGCCACGGCTCCTGCATTGATGGGAAGTGC 2123
    |||||
40 SBJCT: 2040 CATGAACCAGTGCATCGATCCTTCTGTGGGGGGCCACGGCTCCTGCATTGATGGGAAGTGC 2099
    QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCAC 2183
    |||||
45 SBJCT: 2100 CGTGTGTGCAGCTGGCTACAAGGGCGAGCACTGCGAAGAAGTGGATTGCTTGGATCCAAC 2159
    QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243
    |||||
50 SBJCT: 2160 CTGCTCCAGCCATGGTGTCTGTGTGAACGGAGAGTGTCTATGCAGCCCCGGCTGGGGCGG 2219
    QUERY: 2244 TCTGAACTGTGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGCAGTGGGCATGGCACGTA 2303
    |||||
55 SBJCT: 2220 GCTCAACTGCGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGTAGTGGGCATGGCACTTA 2279
    QUERY: 2304 CCTGCCTGACACGGGCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
    |||||
60 SBJCT: 2280 CCTCCCTGACTCTGGCCTCTGCAACTGTGATCCGAATTGGATGGGTCCCGACTGCTCTGT 2339
    QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGAGCCTGCCGCTG 2423
    |||||
    SBJCT: 2340 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGAGCCTGCCGCTG 2399
    QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2483
    |||||
    SBJCT: 2400 TGAAGAGGGCTGGACAGGCGCGGCTTGTGACCAGCGCGTGTGCCACCCCCGCTGCATTGA 2459
    QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
    |||||
    SBJCT: 2460 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2519
    QUERY: 2544 CACCATTG 2551
    |||||
    SBJCT: 2520 CACCATTG 2527

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In this search it was also found that the FCTR3bcd and e nucleic acid had homology to six fragments of *Gallus gallus* partial mRNA for teneurin-2. It has 2780 of 3449 bases (80%) identical to bases 3386-6834, 1553 of 1862 bases (83%) identical to bases 1414-3275, 540 of

QUERY: 6278 GGTATGACGAGACCACCTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCCT 6337
 SBJCT: 6206 GATATGATCTCTACAGGTGTCTTAAAAATGGTGAATTGCAAAGGAGGATTTTCTT 6265
 QUERY: 6338 GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCG 6397
 SBJCT: 6266 GTACAATCCGCTATCGTAAAAATTGGCCCTCTTGTTGACAAACAAATCTACAGATTCTCTG 6325
 QUERY: 6398 AGGAAGGCATGGTCAATGCCAGGTTTGGACTACACCTATCATGACAACAGCTTCGCATCG 6457
 SBJCT: 6326 AAGAAGGTATGGTCAATGCAAGGTTTGATTATACATATCAGACAATAGTTTTCGCATTG 6385
 QUERY: 6458 CAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGTTGACCTCTACCGCTATGATG 6517
 SBJCT: 6386 CAAGCATCAAACCCATCATAAGTGAGACTCCTCTTCCAGTTGATCTTTACCGTTATGATG 6445
 QUERY: 6518 AGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC 6577
 SBJCT: 6446 AGATTTCTGGCAAAGTTGAGCATTTTGGCAAATTTGGAGTTATTTATTATGATATAAATC 6505
 QUERY: 6578 AGATCATCACCCTGCCGTGATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCA 6637
 SBJCT: 6506 AAATTATTACTACAGCAGTTATGACACTGAGTAAGCACTTTGATACCCACGGACGCATTA 6565
 QUERY: 6638 AGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACA 6697
 SBJCT: 6566 AAGAAGTTCAATATGAGATGTTCCGATCCCTGATGTACTGGATGACTGTGCAATATGACA 6625
 QUERY: 6698 GCATGGGCAGGGTGATCAAGAGGGAGCTAAAAGTGGGGCCCTATGCCAATACCACGAAGT 6757
 SBJCT: 6626 GCATGGGAAGAGTAACTAAAAGAGAACTGAAACTTGGGCCGTATGCCAACACAACCAAGT 6685
 QUERY: 6758 ACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGA 6817
 SBJCT: 6686 ATACCTATGATTATGATGGAGATGGGCAATTGCAAAGCGTAGCAGTAAATGATAGGCCTA 6745
 QUERY: 6818 CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTG 6877
 SBJCT: 6746 CCTGGCGTTACAGTTATGACCTGAATGGAAATCTTCACCTCCTGAATCCTGGAAACAGTG 6805
 QUERY: 6878 TGCGCCTCATGCCCTTGCGCTATGACCTC 6906
 SBJCT: 6806 TTCGATTGATGCCCTTGCGCTACGACCTC 6834

SCORE = 1241 BITS (626), EXPECT = 0.0
IDENTITIES = 1553/1862 (83%)
STRAND = PLUS / PLUS

[illegible]

QUERY: 1546 GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 1605
|| ||| ||| ||| || | ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
SBJCT: 1474 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCTCTGAAGTTCAACATA 1533

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QUERY: 1606 TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT 1665
           ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
SBJCT: 1534 TCCCTAGGGAAGGATGCTCTTTTCGGTGTTTATATAAGAAGAGGACTCCCACCATCACAT 1593

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QUERY: 1666 GCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGAGTGTTGAGTCT 1725
|| ||||||| ||||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
SBJCT: 1594 GCACAGTATGATTTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTTGTTGAATCC 1653

QUERY: 1726 CCCAGGGAACGCCGGAGCATACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTCAGTAC 1785
||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
SBJCT: 1654 CCACGGGAACGGCGAAGTATTAGACTCTTGTTTCAAGATGAGGCTGTGTTTGTTTCAGTAC 1713

QUERY: 1786 CTGGATGTGGGCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1845

SBJCT: 1714 TTGGATGTGGGTTTGTGGCACCTGGCGTTTTACAATGATGGCAAGGCAAAAGAAGTGGTC 1773
 QUERY: 1846 TCCTTCAATGTTGTCTAGATTAGTGCAGGACTGTCCACGTATGTCATGGGAAT 1905
 SBJCT: 1774 TCCTTCAGTACAGTTATTTTGGATTAGTGCAGGACTGTCCACGTAAATGTGTCATGGCAAT 1833
 QUERY: 1906 GGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGGATTTCTAGGAGCAGACTGTGCT 1965
 SBJCT: 1834 GGCGAGTGTGTTTCTGGTGTCTGCCACTGTTTCCCAGGATTCATGGAGCAGATTGTGCT 1893
 QUERY: 1966 AAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACAATATTCTAAAGGGACGTGCCAG 2025
 SBJCT: 1894 AAAGCTGCCTGCCCGGTGTGTGCAGTGGCAATGGTCAGTACTCAAAGGAACCTGCTTG 1953
 QUERY: 2026 TGCTACAGCGGCTGGAAAGGTGCAGAGTGCAGCGTGGCCATGAATCAGTGCATCGATCCT 2085
 SBJCT: 1954 TGCTACAGTGGCTGGAAAGGTCCGGAATGTGATGTACCCATCAGCCAGTGTATTGATCCC 2013
 QUERY: 2086 TCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACGTGTCTGCTCTGCTGGCTACAAA 2145
 SBJCT: 2014 TCGTGTGGAGGTCATGGTTCTGCATCGAAGGGAACGTGTCTGTTCCATTGGCTATAAA 2073
 QUERY: 2146 GGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCACCTGCTCCAGCCACGGAGTCTGT 2205
 SBJCT: 2074 GGAGAAACTGTGAGGAAGTTGATTGCTTAGATCCAACATGCTCCAATCACGGGGTCTGT 2133
 QUERY: 2206 GTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGGTCTGAAGTGTGAGCTGGCGAGG 2265
 SBJCT: 2134 GTGAACGGAGAATGTCTCTGCAGCCCAGGCTGGGGTGGAAATAAACTGTGAGCTTCCCAGA 2193
 QUERY: 2266 GTCCAGTGCACAGACAGTGCAGTGGGCATGGCACGTACCTGCCTGACACGGGCCTCTGC 2325
 SBJCT: 2194 GCCCAGTGCACAGACAGTGCAGTGGGCATGGCACATACCTGTCTGACACGGGTCTCTGT 2253
 QUERY: 2326 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGT 2385
 SBJCT: 2254 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCCGTTGAAGTGTGCTCTGTAGACTGT 2313
 QUERY: 2386 GGCACCTACGGCGTCTGCATCGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCA 2445
 SBJCT: 2314 GGCACCCATGGGGTGTGCATTGGCGGAGCGTGTGCTGTGAAGAAGGGTGGACAGGAGTG 2373
 QUERY: 2446 GCGTGTGACCAGCGCTGTGCCACCCCGCTGCATTGAGCACGGGACCTGTAAAGATGGC 2505
 SBJCT: 2374 GCGTGTGACCAGCGTGTGTGTCATCCCGGTGTACAGAGCACGGAACCTGTAAAGATGGG 2433
 QUERY: 2506 AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAACGGCA 2565
 SBJCT: 2434 AAATGTGAATGCAGAGAGGGCTGGAATGGGAGCACTGCACCATTGGTAGGCAAACGACA 2493
 QUERY: 2566 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGT 2625
 SBJCT: 2494 GGCACCGAAACAGATGGCTGCCCTGACTTGTGCAATGGCAACGGGAGGTGCACGCTGGGC 2553
 QUERY: 2626 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCC 2685
 SBJCT: 2554 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCC 2613
 QUERY: 2686 ATGGAACTTCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTG 2745
 SBJCT: 2614 ATGGAACTTCTGTGCCGATAACAAGGATAACGAGGGAGATGGCTTGGTTGACTGCCTA 2673
 QUERY: 2746 GACCCTGACTGCTGCCTGCAGTCAACCTGTCAGAACAGCCTGCTCTGCCGGGGTCCCGG 2805
 SBJCT: 2674 GTCCAGATTGCTGCCTCCAGTCCACTTGTCAAAACAGCCTGCTGTGCCGGGGTCCCGC 2733
 QUERY: 2806 GACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTAT 2865
 SBJCT: 2734 GATCCTCTTGACATCATACAACAGAGCCATTCTGGTTCACCAGCTGTGAAGTCATTCTAT 2793

QUERY: 2032 DKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLYRDEISGKVEHFGKF 2091
 SBJCT: 2101 DKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPIISETPLPVDLYRDEISGKVEHFGKF 2160
 5 QUERY: 2092 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKL 2151
 SBJCT: 2161 GVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVTKRELKL 2220
 10 QUERY: 2152 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXXXXSVRLMPLRYDLRD 2211
 SBJCT: 2221 GPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGNLHLLNPGNSVRLMPLRYDLRD 2280
 15 QUERY: 2212 RITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWSVQYRYDGVGRRASYSK 2271
 SBJCT: 2281 RITRLGDIPYKIDDDGFLCQRGSDVFEYNSKGLLTRAYNKANGWNVQYRYDGLGRRASCK 2340
 20 QUERY: 2272 TNLGHHLLQYFYSDLHNPTRITHVYNHSNSEITSLYDYLQGHLFAMESSSGEYYVASDNT 2331
 SBJCT: 2341 TNLGHHLLQYFYADLHNPTRVTHVYNHSNSEITSLYDYLQGHLFAMESSSGEYYVASDNT 2400
 25 QUERY: 2332 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDV 2391
 SBJCT: 2401 GTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQLVIGFHGGLYDPLTKLVHFTQRDYDV 2460
 30 QUERY: 2392 LAGRWTSPDYTMWKNVKGEPAPFNLYMFKSNNPLSSELDLKNYVTDVKSWLVMFGFQLSN 2451
 SBJCT: 2461 LAGRWTSPDYTMWKNIGREPAPFNLYMFKSNNPLSNELDLKNYVTDVKSWLVMFGFQLSN 2520
 35 QUERY: 2452 IIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNAFMALEGQVITKKLHAS 2511
 SBJCT: 2521 IIPGFPRAKMYFVSPPYELTESQACENGQLITGVQQTTERHNAFMALEGQVISKRLHAS 2580
 40 QUERY: 2512 IREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYS 2571
 SBJCT: 2581 IREKAGHWFATSTPIIGKGIMFAVKKGRVTTGISSIAATDDSRKIASVLNSAHYLEKMHYS 2640
 45 QUERY: 2572 IEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESQVNVTVSQPTLLVNGRTRRFTNIEFQY 2631
 SBJCT: 2641 IEGKDTHYFVKIGSADSDLVTLAMTSGRKVLDSGVNVTVSQPTLLINGRTRRFTNIEFQY 2700
 QUERY: 2632 STLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARDGREGSRLWTEGEKQQ 2691
 SBJCT: 2701 STLLINIRYGLTADTLDEEKARVLDQARQALGSAWAKEQQKARDGREGSRVWTDGEKQQ 2760
 50 QUERY: 2692 LLSTGRVQGYEGYGYVLPVEQYPELADSSSNIQFLRQNMKGK 2733
 SBJCT: 2761 LLNTGRVQGYEGYGYVLPVEQYPELADSSSNIQFLRQNMKGK 2802

The FCTR3bcde and f amino acid sequences have 1524 of 2352 amino acid residues
 (64%) identical to, and 1881 of 2532 residues (79%) positive with, the amino acid residues 429-
 2771, 93 of 157 residues (59%) identical to and 118 of 157 residues (74%) positive with amino
 acid residues 1-155, and 59 of 152 residues (38%) identical to and 68 of 152 residues (43%)
 positive with amino acid residues 211-361 of Ten-m4 [*Mus musculus*] (ptnr: GenBank Acc:
 BAA77399.1) (SEQ ID NO:70) (Table 3R).

Table 3R. BLASTP of FCTR3b, c, d, e, and f against *Mus musculus* Ten-m4 - (SEQ ID NO:70)

>GI|4760782|DBJ|BAA77399.1| (AB025413) TEN-M4 [MUS MUSCULUS]
 LENGTH = 2771
 SCORE = 3089 BITS (8008), EXPECT = 0.0

IDENTITIES = 1524/2352 (64%), POSITIVES = 1881/2352 (79%), GAPS = 28/2352 (1%)

QUERY: 401 KNSSIDSGE GRRVTQEVPPGVFWRSQIHISQPQFLKFNISLGR LFGVYIRRLPP 460
++| ||||| +||| +|++|| ||||| + | | |||||+||| || |+| +|||
5 SBJCT: 429 EDSFIDSGEIDVGRRASQKIPPGTFWRSQVFIIDHPVHLKFNVSLGKAALVGIYGRKGLPP 488

QUERY: 461 SHAQYDFMERLDGK-----EKWSVSPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYND 515
|| |+|+| |||+ | + | + | +| |+||| |+||| |||
10 SBJCT: 489 SHTQFDFVELLDGRRLLTQEARSLGEPQRQSRGPVPPSSHETGFIQYLDSGIWHLAFYND 548

QUERY: 516 GKDKEMVSFNTVVLDSVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQ 575
||+ |+||| | ++|| +|| ||+|||+|+|| ||| ||| | |+|+||| |||
15 SBJCT: 549 GKESVVSFLTTAIESVDNCPSCNYGNGDCISGTCHCFLGFLGPDCGRASCPVLCSGNGQ 608

QUERY: 576 YSKGTCQCYSGWKGAECDVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEEVDCLDPT 635
| | | |+||| ||||| ||||| +| ||+|| | |+|+ ||||| |||||+|||
20 SBJCT: 609 YMKGRCLCHSGWKGAECDVPTNQCIDVACSSHGTICIMGTICNPGYKGESCEEVD CMDPT 668

QUERY: 636 CSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSV 695
||| |||| ||| | |||| ||| | | |||||+||| |||+|||+| | |||+
25 SBJCT: 669 CSSRGVCVRGECHCSVGWGGTNCETPRATCLDQCSGHGTFLPDTGLCNCDPSWTGHDCSI 728

QUERY: 696 EVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTCCKDGKCECREGWNGEHC 755
|+|+ ||| ||||+||| ||||+||| ||||| |||||+||| ||||| |||||
30 SBJCT: 729 EICAADCGHGVCVGGTCRCEDGWMGAACDQRACHPRCAEHGTCDRGKCECSPGWNGEHC 788

QUERY: 756 TIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEG 815
|| +||| ||||| ||| | |||| |||| |||+ +||| | | |||+|
35 SBJCT: 789 TIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHVCVQLGWRGTGCDTSMETGCGDGKDNNDG 848

QUERY: 816 DGLVDCCLPDCLQSACQNSLLCRGSRDPLDIIQQGQT--DWPVAKSFYDRIKLLAGKDS 873
||| |||+||| ||| + ||| |||||+| | + ||||| | |+||
40 SBJCT: 849 DGLVDCMDPDCLQLCHVNPLCLGSPDPLDIIQETQAPVSQQNLNPFYDRIKFLVGRDS 908

QUERY: 874 THIIIPGENPFNSSLVSLIRGQVVTDDGTPLVGVNVSVFKYPKYGYTITRDGTFDLIANG 933
|| |||||+ +|||+|+||| |||||+||| + |||||+|||+|||+ ||
45 SBJCT: 909 THSIIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFINNPLFGYTISRQDGSFDLVTNG 968

QUERY: 934 GASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIIIS 993
| |+ | |||||++|| |+|||+ |+ |+|+||| ||| ||||| | |||++ |
50 SBJCT: 969 GISIILRFERAPFITQEHTLWLPWDRFFVMTIVMRHEENEIPSCDLSNFARPNPVVSPS 1028

QUERY: 994 PLSTFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPL 1053
||++| |+ + ||||| | ||| + | ++| ||||| |||||+|||++| |+|
55 SBJCT: 1029 PLTSFASSCAEKGPIVPEIQALQEEI VIAGCKMRLSYLSSRTPGYKSVLRISLTHPTIPF 1088

QUERY: 1054 NLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYQORVYGLSDAVVSVGFYEYETCP 1113
||++||| ||||| ||+| | |+|+|+ ||||| | |+|+| |+| |||||+|||+||
60 SBJCT: 1089 NLMKVHLMVAVEGRFRKWFAPDLSEYFIWDKTDVYNQKVFGFSEAFVSVGYEYESCP 1148

QUERY: 1114 SLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTTGENQFLTQPPAIITSI 1173
||| |||||+|||+||| | ||||| |||||++||| |||||++||| +| ||
65 SBJCT: 1149 DLILWEKRTAVLQGYEIDASKLGGWSLDKHHALNIQSGILHKGNGENQFVSQPPVIGSI 1208

QUERY: 1174 MGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFPSRNVTSILEL 1233
||| ||||| |||||+||| ||||| | ||||| ||||| |||||+|||+|||+
70 SBJCT: 1209 MGNGRRRSISCPSCNGLADGNKLLAPVALTCGSDGSLYVGDFNYIRRIFFPSGNVTNILEM 1268

QUERY: 1234 RNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGE 1293
|||+|+|||+||| |||+|++||| |||||++||| + ||| ||||| |||||+
75 SBJCT: 1269 RNKDFRHSHPAHKYYLATDPMGAVFLSDTNSRRVFKVKSTTVVKDLVKNSEVVAGTGD 1328

QUERY: 1294 QCLPFDEARCGDGGKAI DATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSND 1353
||| |||+ ||||| +||| +||| ||| |+||| |||||+||| ||||| |||||
80 SBJCT: 1329 QCLPFDDTRCGDGGKATEATLTNPRGITVDKFLIYFVDGTMIRRVQNGIISTLLGSND 1388

QUERY: 1354 LTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPM 1413
||+ ||||| ||++||| |||||+||| |||||+|||+|||+|||+|||+|||
85 SBJCT: 1389 LTSARPLSCDSVMEISQVRLEWPTDLAINPMDNSLYVLDNNVVLQISENHQVRIVAGRPM 1448

QUERY: 1414 HCQVPGID-YSLSKXXXXXXXXXXXXXXXXXGTGVLYITETDEKKINRQVTTNGEICLL 1472
 SBJCT: 1449 HCQVPGIDFSSKVAIHATLESATALAVSHNGVLYIAETDEKKINRQVTTSGEISLV 1508
 5 QUERY: 1473 AGAASXXXXXXXXXXSYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKN 1532
 SBJCT: 1509 AGAPSGCDCKNDANCDGSGDDGYAKDAKLTNPSSLAVCADGELYVADLGNIRIRFIRKN 1568
 10 QUERY: 1533 KPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNVDTELIDNNG 1592
 SBJCT: 1569 KPFLNTQNMVELSSPIDQELYLFDTSKGHLYTQSLPTGDYLYNFTYTGDGDITHITDNG 1628
 15 QUERY: 1593 NSLKIRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVSTQNLELGLMTYDGNTGLLATKS 1652
 SBJCT: 1629 NMVNVRDSTGMPLWLVPDQGVYVWMTGNSALRSVTTQGHELAMMTYHGNSGLLATKS 1688
 20 QUERY: 1653 DETGWTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTVITNLSSV 1712
 SBJCT: 1689 NENGWTTTFEYDSFGRLTNVTFPTQGVSSFRSDTSSVHVQVETSSK-DDVTITTNLSAS 1747
 25 QUERY: 1713 EASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPME 1772
 SBJCT: 1748 GAFYTLQDQVRNSYYIGADGSLRLLLANGMEVALQTEPHLLAGTVNPTVGKRNVTLPID 1807
 30 QUERY: 1773 NGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRRIY 1832
 SBJCT: 1808 NGLNLVEWRQRKEQARGQVTVFGRRLRVHNRNLLSLDFDRVTRTEKIYDDHRKFTLRILY 1867
 35 QUERY: 1833 DQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS 1892
 SBJCT: 1868 DQAGRPSLWSPSSLRNGVNVYTSPGGHIAGIQRGIMSERMEYDQAGRITSRIFADGKMWS 1927
 40 QUERY: 1893 YSYLDKSMVLLQSQRQYIFEYDSSDRLLAVTMPSPVARHSMSTHTSIGYIRNIYNPPESN 1952
 SBJCT: 1928 YTYLEKSMVLHLHSQRQYIFEFDKNDRLSSVTMPNVARQTLETIRSVGYRNIYQPPEGN 1987
 45 QUERY: 1953 ASVIFDYSDDGRILKTSFLGTGRQVFKYKGLSKLSEIVYDSTAVTFGYDETTGVLMNVN 2012
 SBJCT: 1988 ASVIQDFTEDGHLLHTFYLGTGRRVYIKYKGLSKLAETLYDTTKVSFTYDETAGMLKTVN 2047
 50 QUERY: 2013 LQSGGFSTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLP 2072
 SBJCT: 2048 LQNEGFTCTIRYRQIGPLIDRQIFRFTTEGMVNARFDYNY-DNSFRVTSMQAVINETPLP 2106
 55 QUERY: 2073 VDLRYRYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRIKEVQYEMFRSLMY 2132
 SBJCT: 2107 IDLYRYDDVSGKTEQFGKFGVIYYDINQIITAVMTHTKHFDAYGRMKEVQYEIFRSLMY 2166
 60 QUERY: 2133 WMTVQYDSMGRVIKRELKLGYPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXX 2192
 SBJCT: 2167 WMTVQYDNMGRVVKELKVGYPYANTTRYSEYDADGQLQTVSINDKPLWRYSYDLNGLH 2226
 65 QUERY: 2193 XXXXXSVRLMPLRYDLRDIRLGDVQYKIDDDGYLCQGRGSDIFEYNSKGLLTRAYNKA 2252
 SBJCT: 2227 LLSPGNSARLTPLRYDLRDIRLGDVQYKMDDEDGFLRQGGDVFEYNSAGLLIKAYNRA 2286
 70 QUERY: 2253 SGWSVQYRYDGVGRRASYKTNLGHHLQFYSDLHNPTRITHVYNHNSSEITSLYYDLQGH 2312
 SBJCT: 2287 SGWSVRYRYDGLGRRVSSKSSHHLQFFYADLTNPVKVTHLYNHSSSEITSLYYDLQGH 2346
 QUERY: 2313 LFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHG 2372
 SBJCT: 2347 LFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNPNFQIIIGYHG 2406
 65 QUERY: 2373 GLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEP-APFNLYMFKSNPNLSSSELDL 2431
 SBJCT: 2407 GLYDPLTKLVHMGRRDYDVLAGRWTSPDHLELWKRLLSSNSIVPFHLYMFKNNNPISNSQDI 2466
 70 QUERY: 2432 KNYVTDVKSWMFGFQLSNIIIPGFPRAKMYFVPPPYELSESQAS----ENGQLITGVQQ 2487

SCORE = 3295 BITS (8545), EXPECT = 0.0
IDENTITIES = 1695/1 97%), POSITIVES = 1695/1737 (97%)

5 QUERY: 997 TFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI 1056
| | | | |
SBJCT: 1 TFFSAAPGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLLKITMTQSTVPLNLI 60
| | | | |

10 QUERY: 1057 RVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 1116
| | | | |
SBJCT: 61 RVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 120
| | | | |

15 QUERY: 1117 LWEKRTALLQGFEIDPSNLGGWSLDKHHILNVKSGILHKGKTGENQFLTQQPAIITSIMGN 1176
| | | | |
SBJCT: 121 LWEKRTALLQGFEIDPSNLGGWSLDKHHILNVKSGILHKGKTGENQFLTQQPAIITSIMGN 180
| | | | |

20 QUERY: 1177 GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRVNVTISILELRNK 1236
| | | | |
SBJCT: 181 GRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRVNVTISILELRNK 240
| | | | |

25 QUERY: 1237 EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 1296
| | | | |
SBJCT: 241 EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 300
| | | | |

30 QUERY: 1297 PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 1356
| | | | |
SBJCT: 301 PFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 360
| | | | |

35 QUERY: 1357 VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQ 1416
| | | | |
SBJCT: 361 VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQ 420
| | | | |

40 QUERY: 1417 VPGIDYSLSKXXXXXXXXXXXXXXXXXTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 1476
| | | | |
SBJCT: 421 VPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINRLRQVTTNGEICLLAGAA 480
| | | | |

45 QUERY: 1477 SXXXXXXXXXXSYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 1536
| | | | |
SBJCT: 481 SDCDCCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 540
| | | | |

50 QUERY: 1537 NAFNQYEAASPGQEQLYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 1596
| | | | |
SBJCT: 541 NAFNQYEAASPGQEQLYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELIDNNGNSLK 600
| | | | |

55 QUERY: 1597 IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGN TGGLATKSDET G 1656
| | | | |
SBJCT: 601 IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLMTYDGN TGGLATKSDET G 660
| | | | |

60 QUERY: 1657 WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTITNLSSVEASY 1716
| | | | |
SBJCT: 661 WTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDDVTITNLSSVEASY 720
| | | | |

65 QUERY: 1717 TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN 1776
| | | | |
SBJCT: 721 TVVQDQVRNSYQLCNNGTLRVMYANGMGISFHSEPHVLAGTITPTIGRCNISLPMENGLN 780
| | | | |

70 QUERY: 1777 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLR I IYDQVG 1836
| | | | |
SBJCT: 781 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLR I IYDQVG 840
| | | | |

QUERY: 1837 RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSER TDIDKQGRIVSRMFADGK VWSYSYL 1896
| | | | |
SBJCT: 841 RPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSER TDIDKQGRIVSRMFADGK VWSYSYL 900
| | | | |

QUERY: 1897 DKSMVLLQLSQRQYIFEYDSSDRLLAVTMP SVARHSMSTHTSIGYIRNIYNPPESNASVI 1956
| | | | |
SBJCT: 901 DKSMVLLQLSQRQYIFEYDSSDRLLAVTMP SVARHSMSTHTSIGYIRNIYNPPESNASVI 960
| | | | |

QUERY: 1957 FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 2016
| | | | |
SBJCT: 961 FDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 1020
| | | | |

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QUERY: 2017 GFSCITIRY...PLVDKQIYRFSEEGMVNARFDYTYHDNSFRIAS...ISETPLPVDLY 2076
|||||
SBJCT: 1021 GFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 1080

QUERY: 2077 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 2136
|||||
SBJCT: 1081 RYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 1140

QUERY: 2137 QYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXX 2196
|||||
SBJCT: 1141 QYDSMGRVIKRELKLGPIYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHLLNP 1200

QUERY: 2197 XXSVRLMPLRYDLRDRITRLGDRVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 2256
|||||
SBJCT: 1201 GNSVRLMPLRYDLRDRITRLGDRVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 1260

QUERY: 2257 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHFLFAM 2316
|||||
SBJCT: 1261 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHFLFAM 1320

QUERY: 2317 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 2376
|||||
SBJCT: 1321 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYD 1380

QUERY: 2377 PLTKLVHFTQRDYDVLGRWTSPTYMTWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 2436
|||||
SBJCT: 1381 PLTKLVHFTQRDYDVLGRWTSPTYMTWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 1440

QUERY: 2437 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 2496
|||||
SBJCT: 1441 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 1500

QUERY: 2497 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 2556
|||||
SBJCT: 1501 MALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 1560

QUERY: 2557 SVLNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 2616
|||||
SBJCT: 1561 SVLNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 1620

QUERY: 2617 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARD 2676
|||||
SBJCT: 1621 VNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARD 1680

QUERY: 2677 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGK 2733
|||||
SBJCT: 1681 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGK 1737

```

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2528 of 2774 amino acid residues (91%) identical to, and 2557 of 2774 residues (92%) positive with, the 2765 amino acid residue protein neurestin alpha [*Rattus norvegicus*] (GenBank Acc:AF086607) (SEQ ID NO:72), shown in Table 3T.

Table 3T. BLASTP of FCTR3bcd and f against *Rattus norvegicus* Neurestin alpha (SEQ ID NO:72)

```

>GI|9910320|REF|NP_064473.1| NEURESTIN ALPHA [RATTUS NORVEGICUS]
GI|5712201|GB|AAD47383.1|AF086607_1 (AF086607) NEURESTIN ALPHA [RATTUS NORVEGICUS]
LENGTH = 2765

SCORE = 4988 BITS (12938), EXPECT = 0.0
IDENTITIES = 2528/2774 (91%), POSITIVES = 2557/2774 (92%), GAPS = 50/2774 (1%)

QUERY: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDRCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60

```

SBJCT: 1	MDVKDRRH[REDACTED]RGRCGKECRYTSSSLDSEDCRVPTQKYSYSSET[REDACTED]DHDSRMHYGNR	60
QUERY: 61	VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE	120
SBJCT: 61	VTDLVHRESDEF[REDACTED]SRQGANFTLAELGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTE	120
QUERY: 121	GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTXXXXXXXXXXXXXGRXXXXXXXXXXXXX	180
SBJCT: 121	GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTDSDNENKSDDDNGRPIPTSSSSLL	180
QUERY: 181	XXXXXXXXXHNPPPVSCQMPLLDSENTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXXX	240
SBJCT: 181	PSAQLPSSHNP[REDACTED]PVSCQMPLLDSENTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP	240
QUERY: 241	NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPE[REDACTED]	300
SBJCT: 241	NHHSQSTLRPPLPPPHNHTLSHHSSANSLN[REDACTED]SLTNRRSQIHAPAPAPNDLATTPE[REDACTED]	300
QUERY: 301	LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK	360
SBJCT: 301	LQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK	360
QUERY: 361	AFKLLKPSKYCSWKCXXXXXXXXXXXXXXXXXXFYI-----	395
SBJCT: 361	AFKLLKPSKYCSWKCAALSAIAAALLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT	420
QUERY: 396	-----VPWSLKNSSIDSGAEVGR[REDACTED]VTQEVPPGVFWRSQIHISQPQFLK	439
SBJCT: 421	GLPGNDDVATVP[REDACTED]SGGKVPWSLKNSSIDSGAEVGR[REDACTED]VTQEVPPGVFWRSQIHISQPQFLK	480
QUERY: 440	FNISLGKDALFGVYIRRGLP[REDACTED]PSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	499
SBJCT: 481	FNISLGKDALFGVYIRRGLP[REDACTED]PSHAQYDFMERLDGKEKWSVVESPRERRSIQTLVQNEAVF	540
QUERY: 500	VQYLDVGLWHLAFYNDGDKDEMVSFNTVVLD[REDACTED]SVQDCPRNCHNGECVSGVCHCFPGFLGA	559
SBJCT: 541	VQYLDVGLWHLAFYNDGDKDEMVSFNTVVLD[REDACTED]SVQDCPRNCHNGECVSGVCHCFPGFLGA	600
QUERY: 560	DCAKAACPVLC[REDACTED]SGNGQYSKGT[REDACTED]CQCYSGWKGAECDVPMNQCIDPSCGGHGS[REDACTED]CIDGNCVCSA	619
SBJCT: 601	DCAKAACPVLC[REDACTED]SGNGQYSKGT[REDACTED]CQCYSGWKGAECDVPMNQCIDPSCGGHGS[REDACTED]CIDGNCVCAA	660
QUERY: 620	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDT	679
SBJCT: 661	GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYLPDS	720
QUERY: 680	GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC	739
SBJCT: 721	GLCNCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC	780

QUERY: 740	KDGKCECREGWNGEHCTIGRQTAGTETDGC[REDACTED]PDL[REDACTED]CNGNGRCTLGQNSWQCVCQTGWRGPGC	799
SBJCT: 781	KDGKCECREGWNGEHCTI-----DGCPDL[REDACTED]CNGNGRCTLGQNSWQCVCQTGWRGPGC	831
QUERY: 800	NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDI IQQGQTDWPAVK	859
SBJCT: 832	NVAMETSCADNKDNEGDGLVDCLDPDCCLQSACQNSLLCRGSRDPLDI IQQGQTDWPAVK	891
QUERY: 860	SFYDRIKLLAGKDSTHIIPGENPFNSSLVSLIRGQVTTDGTPLVGVNV[REDACTED]SFVKYPKYGYT	919
SBJCT: 892	SFYDRIKLLAGKDSTHIIPGDNPFNSSLVSLIRGQVTTDGTPLVGVNV[REDACTED]SFVKYPKYGYT	951
QUERY: 920	ITRQDGTFDLIANGGASLT[REDACTED]LHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD	979
SBJCT: 952	ITRQDGTFDLIANGGASLT[REDACTED]LHFERAPFMSRERTVWPPWNSFYAMDTLVMKTEENSIPSCD	1011
QUERY: 980	LSGFVRPDPII[REDACTED]SSPLSTFFSAA[REDACTED]PGQNPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYK	1039
SBJCT: 1012	LSGFVRPDPII[REDACTED]SSPLSTFFSAA[REDACTED]NPIVPETOVLHEEIELPGTNVKLRYLSSRTAGYK	1071

QUERY: 1040 SLLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLASTFIIDAYGQRVYGLS 1099
 |||||
 SBJCT: 1072 SLLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1131
 |||||
 QUERY: 1100 DAVVSVGFYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGKTGE 1159
 |||||
 SBJCT: 1132 DAVVSVGFYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILLKGTGE 1191
 |||||
 QUERY: 1160 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219
 |||||+|||
 SBJCT: 1192 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFNYIR 1251
 |||||
 QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
 |||||+|||+|||
 SBJCT: 1252 RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1311
 |||||
 QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
 |||||+|||
 SBJCT: 1312 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 1371
 |||||
 QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
 |||||
 SBJCT: 1372 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1431
 |||||
 QUERY: 1400 TENHQVSI IAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXGTGVLYITETDEKKINR 1459
 |||||
 SBJCT: 1432 TENHQVSI IAGRPMHCQVPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINR 1491
 |||||
 QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXSYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
 |||||
 SBJCT: 1492 LRQVTTNGEICLLAGAASDCCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1551
 |||||
 QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPGQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1579
 |||||
 SBJCT: 1552 DLGNIRIRAVSKNKPVLNAFNQYEAASPGQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1611
 |||||
 QUERY: 1580 TDNDVTELDIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTGTVNGGLKVVSTQNLGLM 1639
 |||||
 SBJCT: 1612 ADNDVTELDIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTGTVNGGLKAVSTQNLGLM 1671
 |||||
 QUERY: 1640 TYDGNTGLLATKSDEGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
 |||||+|||
 SBJCT: 1672 TYDGNTGLLATKSDEGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITVDIENSNR 1731
 |||||
 QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
 |+|||+|||+|||+|||
 SBJCT: 1732 DNDVTVITNLSSVEASYTVVQDQVRNSYQLCSNGTLRVMYANGMGVSVFHSEPHVLAGTIT 1791
 |||||
 QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
 |||||
 SBJCT: 1792 PTIGRCNISLPMENGLNSIEWRLRKEQIKGVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1851
 |||||
 QUERY: 1820 YDDHRKFTLRRIIDYQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1879
 |||||
 SBJCT: 1852 YDDHRKFTLRRIIDYQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGR 1911
 |||||
 QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLQLSQRQYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1939
 |||||
 SBJCT: 1912 IVSRMFADGKVWSYSYLDKSMVLLQLSQRQYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1971
 |||||
 QUERY: 1940 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
 |||||
 SBJCT: 1972 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2031
 |||||
 QUERY: 2000 GYDETTGVLKMNVLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059
 |||||+|||+|||
 SBJCT: 2032 GYDETTGVLKMNVLQSGGFSCTIRYRKVGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2091
 |||||
 QUERY: 2060 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRI 2119
 |||||

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|||||
5  SBJCT: 2092 ASIKPVISEPVDLYRYDEISGKVEHFGKFGVIYYDINQIITLSKHFDTHGRI 2151
    QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2179
    SBJCT: 2152 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGPYANTTKYTYDYDGDGQLQSVAVNDRP 2211
    QUERY: 2180 TWRYSDYXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
10  SBJCT: 2212 TWRYSYDLNGLNHLNPGNSARLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2271
    QUERY: 2240 NSKGLLTRAYNKASGWSVQYRYDGVGRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
    SBJCT: 2272 NSKGLLTRAYNKASGWSVQYRYDGVSRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2331
15  QUERY: 2300 SEITSLYYDLQGHLFAMESSSGEEYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359
    SBJCT: 2332 SEITSLYYDLQGHLFAMESSSGEEYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2391
    QUERY: 2360 SNPDMFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMF 2419
    SBJCT: 2392 SNPDMFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWRNVGKEPAPFNLYMF 2451
20  QUERY: 2420 KSNPNLSSELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479
    SBJCT: 2452 KNNNPLSNELDLKNYVTDVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2511
25  QUERY: 2480 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
    SBJCT: 2512 QLITGVQQTTERHNQAFMALEGQVISKKLHAGIREKAGHWFATTTPIIGKGIMFAIKEGR 2571
30  QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVKIGSADGDLVTLGTTIGR 2599
    SBJCT: 2572 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVKIGAADGDLVTLGTTIGR 2631
35  QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
    SBJCT: 2632 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2691
40  QUERY: 2660 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2719
    SBJCT: 2692 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSS 2751
45  QUERY: 2720 SNIQFLRQNEMGKR 2733
    SBJCT: 2752 SNIQFLRQNEMGKR 2765

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* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

50 The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2536 of 2774 amino acid residues (91%) identical to, and 2558 of 2774 residues (91%) positive with, the 2764 amino acid residue protein Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc:NP_035986.2) (SEQ ID NO:65), shown in Table 3U.

Table 3U. BLASTP of FCTR3bcde and f against Odd Oz/ten-m homolog 2 (SEQ ID NO:65)

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55 >GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M HOMOLOG
    3 (DROSOPHILA) [MUS MUSCULUS]
    60 GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]
        LENGTH = 2764
    SCORE = 4996 BITS (12961), EXPECT = 0.0

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QUERY: 980 LSGFVRPDPIISSPLSTFFSAAPGQNPIVPETQVLHEEIELPGSNRYLSSRTAGYK 1039
 SBJCT: 1011 LSGFVRPDPIISSPLSTFFSASPASNPIVPETQVLHEEIELPGTNRYLSSRTAGYK 1070
 5 QUERY: 1040 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099
 SBJCT: 1071 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1130
 10 QUERY: 1100 DAVSVSGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTE 1159
 SBJCT: 1131 DAVSVSGFEYETCPSLILWEKRTALLQGFELDPSNLGGWSLDKHTLNVKSGILHKGTE 1190
 QUERY: 1160 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGFDFNYIR 1219
 15 SBJCT: 1191 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFDFNYIR 1250
 QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
 SBJCT: 1251 RIFPSRNVTSILELRNKEFKHSNPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1310
 20 QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
 SBJCT: 1311 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 1370
 25 QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
 SBJCT: 1371 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1430
 30 QUERY: 1400 TENHQVSI IAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXXGVLVITETDEKKINR 1459
 SBJCT: 1431 TENHQVSI IAGRPMHCQVPGIDYSLSKLAIHSALESASAIAISHTGVLVITETDEKKINR 1490
 QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXXXXSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
 35 SBJCT: 1491 LRQVTTNGEICLLAGAASDCCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1550
 QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPEQEYLVFNADGIHQYTVSLVTGEYLYNFTYS 1579
 SBJCT: 1551 DLGNIRIRAVSKNKPVLNAFNQYEAASPEQEYLVFNADGIHQYTVSLVTGEYLYNFTYS 1610
 40 QUERY: 1580 TDNDVTEIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTTNGGLKVVSTQNLELGLM 1639
 SBJCT: 1611 ADNDVTEIDNNGNSLKIRRDSSGMPRHLLMPDNQIITLTVGTTNGGLKAVSTQNLELGLM 1670
 45 QUERY: 1640 TYDGNTGLLATKSDGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
 SBJCT: 1671 TYDGNTGLLATKSDGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1730
 50 QUERY: 1700 DDDVTIVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
 SBJCT: 1731 DDDVTIVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMAVSFHSEPHVLAGTIT 1790
 QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
 55 SBJCT: 1791 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1850
 QUERY: 1820 YDDHRKFTLRRIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSSERTDIDKQGR 1879
 SBJCT: 1851 YDDHRKFTLRRIYDQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSSERTDIDKQGR 1910
 60 QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLQLSQRYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1939
 SBJCT: 1911 IVSRMFADGKVWSYSYLDKSMVLLQLSQRYIFEYDSSDRLLHAVTMPVARHSMSTHTSI 1970
 65 QUERY: 1940 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
 SBJCT: 1971 GYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2030
 70 QUERY: 2000 GYDETTGVLKMNVLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059
 SBJCT: 2031 GYDETTGVLKMNVLQSGGFSCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2090

kinase implicated in breast and prostate cancer progression that was originally identified in rat neuro/glioblastoma cell lines. Extopic expression of HER-2/ErbB2/NEU in MDA-MB-435 breast adenocarcinoma cells confers chemoresistance to Taxol-induced apoptosis relative to vector transfected control cells (Yu et al. Overexpression of ErbB2 blocks Taxol-induced apoptosis by up-regulation of p21Cip1, which inhibits p34Cdc2 kinase. Molec. Cell 2: 581-591, 1998).

FCTR3 related tenascins and cancer biology

As mentioned, FCTR3 also has significant homology to DOC4, (AKA tenascin M), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The tenascins are a growing family of extracellular matrix proteins that play prominent roles in tissue interactions critical to embryogenesis. Overexpression of tenascins has been described in multiple human solid malignancies.

The role of the tenascin family of related proteins is to regulate epithelial-stromal interactions, participate in fibronectin-dependent cell attachment and interaction. Indeed, tenascin-C (TN) is overexpressed in the stroma of malignant ovarian tumours particularly at the interface between epithelia and stroma leading to suggestions that it may be involved in the process of invasion (Wilson et al (1996) Br J Cancer 74: 999-1004). Tenascin-C is considered a therapeutic target for certain malignant brain tumors (Gladson CL : J Neuropathol Exp Neurol 1999 Oct;58(10):1029-40). Stromal or moderate to strong periductal Tenascin-C expression in DCIS (ductal carcinoma in situ) correlates with tumor cell invasion. (Jahkola et al. Eur J Cancer 1998 Oct;34(11):1687-92. Tenascin-C expression at the invasion border of early breast cancer is a useful predictor of local and distant recurrence. Jahkola T, et al. Br J Cancer. 1998 Dec;78(11):1507-13). Tenascin (TN) is an extracellular matrix protein found in areas of cell migration during development and expressed at high levels in migratory glioma cells. Treasurywala S, Berens ME Glia 1998 Oct;24(2):236-43 Migration arrest in glioma cells is dependent on the alphaV integrin subunit. Phillips GR, Krushel LA, Crossin KL J Cell Sci 1998 Apr;111 (Pt 8):1095-104 Domains of tenascin involved in glioma migration. Finally, tenascin expression in hormone-dependent tissues of breast and endometrium indicate that Tenascin expression reflects malignant progression and is down-regulated by antiprogestins during terminal differentiation of rat mammary tumors (Vollmer et al. Cancer Res 1992 Sep 1;52(17):4642-8)

Potential role of FCTR3 in oncologic disease progression:

Based on the bioactivity described in the medical literature for related molecules, FCTR3 may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components. In consideration, FCTR3 may play a role in the following malignant properties:

- Autocrine/paracrine stimulation of tumor cell proliferation
- Autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy
- Local tissue remodeling, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis.
- Tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance.

Therapeutic intervention targeting FCTR3 in oncologic and central nervous system indications:

Predicted disease indications from expression profiling in 41 normal human tissues and 55 human cancer cell lines (see Example 2) include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas. Targeting of FCTR3 by human or humanized monoclonal antibodies designed to disrupt predicted interactions of FCTR3 with its cognate ligand may result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Identification of small molecules that specifically/selectively interfere with downstream signaling components engaged by FCTR3/ligand interactions would also be expected to result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Likewise, modified antisense ribonucleotides or antisense gene expression constructs (plasmids, adenovirus, adeno-associated viruses, "naked" DNA approaches) designed to diminish the expression of FCTR3 transcripts/messenger RNA (mRNA) would be anticipated based on predicted properties of FCTR3 to have anti-tumor impact.

Based on the relatedness to neurestin and heregulins, as well as its high level expression in brain tissue, FCTR3 may also be used for remyelination in order to promote regeneration/repair/remyelination of injured central nervous system cells resulting from ischemia, brain trauma and various neurodegenerative diseases.. This postulate is based on reports indicating that neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis (Cannella et al. .

Proc. Nat. Acad. Sci. 95: 10100-10105, 1998). The expression of the related molecule neurestin can be induced in external plexus cells during regeneration of olfactory sensory neurons.

FCTR4

FCTR4 is a plasma membrane protein related to NF-Kappa-B P65delta3 protein. The clone is expressed in fetal liver tissues.

The novel FCTR4 nucleic acid of 609 nucleotides (also referred to as 29692275.0.1) is shown in Table 4A. An ORF begins with an ATG initiation codon at nucleotides 99-101 and ends with a TAA codon at nucleotides 522-524. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 4A, and the start and stop codons are in bold letters.

Table 4A. FCTR4 Nucleotide Sequence (SEQ ID NO:14)

CTGACATACTATATTAGTTGTTTGGTTCCTGCTCTCCACTCCAGCTAGAATATAAGTTCCATAGGGCAGAGTTTTGTTCA
CTGCTATATTTTATAAGCATGAATGAATGCATGAACGAATGGACTGATAACCCACAAGCCAAAGACCTCCATGACCTGCC
ACTGCCCTCCTTTTCAATTTTATTCTCACCTCTACCAATACTAAATCACCTAGTTATGTAAATACGATATGCATTTTCATGG
CCCCTTGCTTTGTTCATATGCTGTTCCCTTTGCCTGGAATATAAACTCTCAAAATACCATCCACATTTTAAATCTTCTCC
AGAAAGCTTCCTCTGTCCACCCCCACCTCCCACCCCCATATAGAGTAAGTCAGTCTTTCTTTGTGCTACATTTGTACC
TGTATCTACAGTGGCTCTAATCAAATGCACTGTGTCTCTCACTTCCCTAGATTGTGAATCTTTGAGGCTGAAGACTACT
TATTCATCTCTTTACCTCCAATGCCTAGGACAGGACCTTCATAAAGCAACTACTCTATAAATGTTGAAACATATGCATGA
CTATTCTGTAACAGGAATGAAAATATGGCATTTCAAGAAGTCACTACTC

The FCTR4 protein encoded by SEQ ID NO:14 has 141 amino acid residues and is presented using the one-letter code in Table 4B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the plasma membrane with a certainty of 0.6000. The most likely cleavage site for a peptide is between amino acids 39 and 40, *i.e.*, at the dash in the amino acid sequence ACT-CCA, based on the SignalP result. The predicted molecular weight of this protein is 16051.5 Daltons.

Table 4B. Encoded FCTR4 protein sequence (SEQ ID NO:15).

MNECMNEWTDNPQAKDLHDLPLPSFHFILSTNTKSPSYVNTICTFMAPCFVICCSLCLLEYKLSKYHPHFKIFSRKLPPLSTPLPP
PYRVSQSFLCATFVPVSTVALIKLHCVSHFLDCELFEAEDYLFISLPMPRTGPS

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR4 protein showed 30 % identities (22 over 72 amino acids) and 43% homologies (31 over 72 amino acids) with hypothetical 10 kD protein of *Trypanosoma cruzi* (86 aa; ACC:Q99233) shown in Table 4C. The best homologies with a human protein were 54 % identities (114 over 343 amino acids) with NF-Kappa-B P65delta3 protein (71 aa fragment; ACC:Q13313) (SEQ ID NO:77).

Table 4C. BLASTP of FCTR4 against protein sequences

BLAST X search results are shown below:

ptrn:SPTREMBL-ACC:Q99233 HYPOTHETICAL 10 KD PROTEIN +3, 68, 0.60, 1, (SEQ ID

NO:73)

ptnr:SPTREMBL-ACC:Q16896 GABA RECEPTOR SUBUNIT - AEDES +3, 66, 0.81, 4 (SEQ ID NO:74)

ptnr:SPTREMBL-ACC:O76473 GABA RECEPTOR SUBUNIT - LEPTI... +3, 66, 0.99, 2 (SEQ ID NO:75)

ptnr:TREMBLNEW-ACC:AAD28317 F13J11.13 PROTEIN - Arabid... +3, 62, 0.99, 1 (SEQ ID NO:76)

Based upon homology, FCTR4 proteins and each homologous protein or peptide may share at least some activity.

FCTR5

FCTR5 is a protein bearing sequence homology to human complement C1R component precursor. The clone is expressed in breast, heart, lung, fetal lung, salivary gland, adrenal gland, spleen, kidney, and fetal kidney.

The novel FCTR5 nucleic acid of 1667 nucleotides (also referred to as 32125243.0.21) is shown in Table 5A. An ORF begins with an ATG initiation codon at nucleotides 34-36 and ends with a TGA codon at nucleotides 1495-1497. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 5A, and the start and stop codons are in bold letters.

Table 5A. FCTR5a Nucleotide Sequence (SEQ ID NO:16)

GTTCTCTCGCAGGTCCCAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCCCTCA
CTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCTCCAGGCTTGCCCCAACCCGGGGCTCCGTCC
TCTTGGCCCAAGAGCTACCCAGCAGCTGACATCCCCCGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCAG
GACATCAAGGCTCCAGAGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTGCAGG
GGACTCTGTCAATCTCATTTCGTTCGGTTCGGATCCAAGCCAGTTCTGTGGTCAGCAAGGCTCCCTCTGGGCAGGCCCC
CTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTTTGGCGCTGACCTTCCGCACACAGCCTTCTCGGAGAACAAGACT
GCCCACCTCCACAAGGGCTTCTGGCCCTCTACCAAACCGTGGCTGTGAACCTATAGTCAGCCCATCAGCGAGGCCAGCAG
GGGCTCTGAGGCCATCAACGCACCTGGAGACAACCTGCCAAGGTCCAGAACCACTGCCAGGAGCCCTATTATCAGGCCG
CGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGACCTGGAAAGACAGACAGGATGGGGAGGAGTTCTTCAGTGTATG
CCTGTCTGCGGACGGCCAGTCACCCCATTTGCCCAGAATCAGACGACCTCGGTTCTTCCAGAGCCAAGCTGGGCAACTT
CCCCTGGCAAGCCTTCACAGTATCCACGGCCGTGGGGCGGGGCCCTGCTGGGGACAGATGGATCCTCACTGCTGCCC
ACACCATCTACCCCAAGGACAGTGTCTCTCAGGAAGAACCAGAGTGAATGTGTTCTTGGGCCACACAGCCATAGAT
GAGATGCTGAAACTGGGAACCACTGTCCACCGTGTGCTGTGACCCCGACTACCGTCAGAATGAGTCCATAACTT
TAGCGGGACATCGCCCTCTGGAGTGCAGCACAGCATCCCCCTGGGCCCAACGTCCTCCCGGTCTGTCTGCCCGATA
ATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACGTGAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTG
AAGTACTCGAGGCTGCCTGTAGCTCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGTTTTT
TGACAAATATGTTCTGTGTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGGACAGTGGCAGCCTCTATGTGGTAT
GGGACAATCATGCCATCACTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGTATGACTTCTAC
ACCAAGGTGCTCAGCTATGTGGAAGTGAATGAAGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGGGACT
GACCAGCACAGTGGAGGCCCGAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACTGGGGTAGGGGTGGGGGTTTTCTCT
TGCAGTGGCTTGGTGAACAGTGATGTAATAGGATTTCCCTTTTTTTTTTTTTTTTTTAAAAAAA

The FCTR5 protein encoded by SEQ ID NO:16 has 487 amino acid residues, and is presented using the one-letter code in Table 5B. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5 protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5B. Encoded FCTR5a protein sequence (SEQ ID NO:17).

MPGPRVWGKYLWRSPhSKGCPGAMWLLLLWGVLAQCPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQDF
DLEPSQDCAGDSVTISFVGSDFPSQFCGQQGSLGRPPGQREFVSSGRSLRLTFRTPSSSENKTAHLHKGFLLALYQTVAVNYSQPI S
EASRGSEAINAPGDNPAKVQNHQEPYQAAAAGALTCATPGTWKDRQDGEEVLQCMFVCGRPVTPIAQNQTLGSSRAKLGNF PW
QAFTSIHGRGGGALLGDRWILTAHTIYPKDSVSLRKNQSVNVFLGHTAIDMLKLGHNHPVHRVVVHPDYRQNESHNFSGDIALLE
LQHSIPLGPNVLPVCLPDNETLYRSGLLYVSGFGMEMGWLTELKYSRLPVAPREACNAWLQKRQRPEVFSNMFVGVDETQRHS
VCQGDGSLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

An alternative embodiment, FCTR5b, is a 1691 base sequence shown in Table 5C.

Table 5C. FCTR5b Nucleotide Sequence (SEQ ID NO:18)

TTTTTTTTTAAAAAAAAAAAAAAAAAGGGAATCCTATTCACATCACTGTTGCACCAAGCCACTGCAAGAGAAACCCCAACCCCT
ACCCAGTGTTCAGTCCTCACTCCAGGCCCTCTGTTGCCTGGGGCCTCCACTGTGCTGGTCAGTCCCTGTTCAAGCCCCCAGGGTC
AATTCTTGCCATTCACTACCTTGTATCCAGTCCACATAGCTGAGCACCTTGGTGTAGAAGTCATACCTTCGCCACACCCATG
CCCCAGGACACAATGCCCGTGGCCACCCAGTGATGGGCATGATTGTCCCATACCATAGAGGCTGCCACTGTCCCCCTGGCAGAC
ACTGTGCTTTTGGCTCTCATCCCCAACACAGAACATATTGTGAGAAACACCTCGGGTCTCTGTCTCTTTTGGAGCCAGCGGTGC
AGGCTCCCTGGGAGCTACAGGCAGCCTCGAGTACTTCAGTCACTAGTTAGCCAGCCATCTCCATGCCAAACCCACTGACGTAG
CCCAACAAGCCGCTGCGGTAGAGGTCTCATTATCGGGCAGACAGACCGGGAGGACGTTGGGGCCAGGGGGATGCTGTGCTGCAG
CTCCAGGAGGGCGATGTCCCCGCTAAAGTTATGGGACTCATTCTGACGGTAGTTCGGGTGCACAACGACACGGTGGACAGGGTGGT
TCCCCAGTTTCAGCATCTCATCTATGGCTGTGTGGCCCAAGAACACATTCACTCTGTTCTTCTGAGAGAAACACTGTCTTGTG
GGGTAGATGGTGTGGGCAGCAGTGAAGATCCATCTGTCCCCCAGCAGGGCCCCCGCCCCACGGCCGTGGATACTGGTGAAGCTTG
CCAGGGGAAGTTGCCAGCTTGGCTCTGGAAGAACCAGGGTTCGTCTGATTCTGGGCAATGGGGGTGACTGGCCGTCCGCAGACAG
GCATACACTGAAGAACCCTCCCCATCCTGTCTGTCTTTCCAGGTCCCTGGGGTTGCACAGGTGAGTGCCCTGCTGCCCGGGCC
TGATAATAGGGCTCCTGGCAGTGGTTCTGGACCTTGGCAGGTTGTCTCCAGGTGCGTTGATGGCCTCAGAGCCCCCTGCTGGCCTC
GCTGATGGGCTGACTATAGTTACAGCCACGGTTTGGTAGAGGGCCAGGAAGCCCTTGTGGAGGTGGGCAGTCTTGTCTCCGAGG
AAGGCTGTGTGCGGAAGGTGAGCCGAACTCCTCCCTGAGGATACAACTCCCTCTGACCAGGGGGCCTGCCAGAGGGGAGCCT
TGCTGACCACAGAACTGGCTTGGATCCGAACCGACGAATGAGATTGTGACAGAGTCCCCCTGCACAGTCTGGGACGGCTCCAGGTC
GAAGTCTTGAAGACGAGCCTCACAGCAAAGCCCTCTGGAGCCTTGATGTCCGTGCTGCTCTCTTGGCCTTTGCCATACGGCTCTG
GGTACCCGGGGGATGTCACTGCTGGGGTAGCTCTTGGGCCAAGAGGACGAGCCCCGGGTGGGCAAGCCTGGAGACTCCCCAG
AGAAGCAGCCACCATGCTGCGCCTGGACAGCCTTGGAGCAGGGCTTCTCCAGAGATATTTCCCCCACACTCTGGGTCCAGGCAT
CTGGAAGTGGACATCTGGGACCTGCGAGAGAACTGGCCAGGATAGGGAACAAAAG

The FCTR5b protein encoded by SEQ ID NO:18 has 487 amino acid residues, and is presented using the one-letter code in Table 5D. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5b protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5D. Encoded FCTR5b protein sequence (SEQ ID NO:19).

MPGPRVWGKYLWRSPhSKGCPGAMWLLLLWGVLAQCPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVFQDF
DLEPSQDCAGDSVTISFVGSDFPSQFCGQQGSLGRPPGQREFVSSGRSLRLTFRTPSSSENKTAHLHKGFLLALYQTVAVNYSQPI S
EASRGSEAINAPGDNPAKVQNHQEPYQAAAAGALTCATPGTWKDRQDGEEVLQCMFVCGRPVTPIAQNQTLGSSRAKLGNF PW
QAFTSIHGRGGGALLGDRWILTAHTIYPKDSVSLRKNQSVNVFLGHTAIDMLKLGHNHPVHRVVVHPDYRQNESHNFSGDIALLE
LQHSIPLGPNVLPVCLPDNETLYRSGLLYVSGFGMEMGWLTELKYSRLPVAPREACNAWLQKRQRPEVFSNMFVGVDETQRHS
VCQGDGSLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR5a protein showed 58 % identities (177 over 302 amino acids) and 74 % homologies (226 over 302 amino acids) with human complement C1R component precursor (EC 3.4.21.41) (705 aa.; ACC:P00736). Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

In a search of sequence databases, it was found, for example, that the nucleic acid sequence the nucleotides 17-1594 of FCTR5a have 1575 of 1578 bases (99 %) identical to *Homo sapiens* complement C1r-like proteinase precursor (GENBANK-ID: XM_007061.1) (SEQ ID NO:78) (Table 5E).

Table 5E. BLASTN of FCTR5a against *Homo sapiens* complement C1r-like proteinase precursor (SEQ ID NO:78)

>GI|11436767|REF|XM_007061.1| HOMO SAPIENS COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, (LOC51279),

MRNA
LENGTH = 3318

SCORE = 3104 BITS (1566), EXPECT = 0.0
IDENTITIES = 1575/1578 (99%)
STRAND = PLUS / PLUS

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QUERY: 17  CAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 76
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 1    CAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 60

QUERY: 77  CTCAC TCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCTCTCCAGG 136
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 61  CTCAC TCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCTCTCCAGG 120

QUERY: 137 CTTGCCCAACCCGGGGCTCCGTCCTCTTGCCCCAAGAGCTACCCAGCAGCTGACATCCC 196
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 121 CTTGCCCAACCCGGGGCTCCGTCCTCTTGCCCCAAGAGCTACCCAGCAGCTGACATCCC 180

QUERY: 197 CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 256
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 181 CCGGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACGGACATCAAGGCTCCAG 240

QUERY: 257 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCAGGACTGTG 316
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 241 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCAGGACTGTG 300

QUERY: 317 CAGGGGACTCTGTCACAATCTCATTCTCGGTTCCGATCCAAGCCAGTTCTGTGGTCAGC 376
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 301 CAGGGGACTCTGTCACAATCTCATTCTCGGTTCCGATCCAAGCCAGTTCTGTGGTCAGC 360

QUERY: 377 AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTGTATCCTCAGGGAGGAGTT 436
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 361 AAGGCTCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTGTATCCTCAGGGAGGAGTT 420

QUERY: 437 TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCACCTCCACAAGG 496
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 421 TGCGGCTGACCTTCCGCACACAGCCTTCCTCGGAGAACAAGACTGCCACCTCCACAAGG 480

QUERY: 497 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 556
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SBJCT: 481 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 540

QUERY: 557 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCTGCCAAGGTCCAGAACCCT 616
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||

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SBJCT: 541 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGTCCAGAACCACT 600
 QUERY: 617 GCCAGGAGCATTATCAGGCCGCGGCAGCAGGGGCACTCACCTCAACCCCAGGGA 676
 SBJCT: 601 GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCCAGGGA 660
 QUERY: 677 CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGATGCCTGTCTGCGGACGGC 736
 SBJCT: 661 CCTGGAAAGACAGACAGGATGGGGAGGAGGTTCTTCAGTGATGCCTGTCTGCGGACGGC 720
 QUERY: 737 CAGTCACCCCCATTGCCAGAATCAGACGACCCTCGGTTCTTCAGAGCCAAGCTGGGCA 796
 SBJCT: 721 CAGTCACCCCCATTGCCAGAATCAGACGACCCTCGGTTCTTCAGAGCCAAGCTGGGCA 780
 QUERY: 797 ACTTCCCTGGCAAGCCTTACCAGTATCCACGCCGTGGGGGCGGGGCCCTGCTGGGGG 856
 SBJCT: 781 ACTTCCCTGGCAAGCCTTACCAGTATCCACGCCGTGGGGGCGGGGCCCTGCTGGGGG 840
 QUERY: 857 ACAGATGGATCCTCACTGCTGCCCACACCATCTACCCAAGGACAGTGTCTCTCAGGA 916
 SBJCT: 841 ACAGATGGATCCTCACTGCTGCCCACACCGTCTACCCAAGGACAGTGTCTCTCAGGA 900
 QUERY: 917 AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 976
 SBJCT: 901 AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAAACTGG 960
 QUERY: 977 GGAACCACCCTGTCCACCGTGTGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA 1036
 SBJCT: 961 GGAACCACCCTGTCCACCGTGTGTTGTGCACCCCGACTACCGTCAGAATGAGTCCCATA 1020
 QUERY: 1037 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAAGC 1096
 SBJCT: 1021 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAAGC 1080
 QUERY: 1097 TCCTCCCGGTCTGTCTGCCCATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1156
 SBJCT: 1081 TCCTCCCGGTCTGTCTGCCCATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1140
 QUERY: 1157 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1216
 SBJCT: 1141 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1200
 QUERY: 1217 CTGTAGCTCCCAGGGAGGCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1276
 SBJCT: 1201 CTGTAGCTCCCAGGGAGGCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1260
 QUERY: 1277 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1336
 SBJCT: 1261 TTTCTGACAATATGTTCTGTGTTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1320
 QUERY: 1337 ACAGTGGCAGCCTCTATGTGGTATGGGACAATCATGCCATCACTGGGTGGCCACGGGCA 1396
 SBJCT: 1321 ACAGTGGCAGCGTCTATGTGGTATGGGACAATCATGCCATCACTGGGTGGCCACGGGCA 1380
 QUERY: 1397 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1456
 SBJCT: 1381 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1440
 QUERY: 1457 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1516
 SBJCT: 1441 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1500
 QUERY: 1517 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1576
 SBJCT: 1501 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1560
 QUERY: 1577 GGGGTAGGGGGTGGGGGT 1594
 SBJCT: 1561 GGGGTAGGGGTGGGGGT 1578

In this search it was also found that the FCTR5a nucleic acid had homology to three fragments of *Homo sapiens* complement component 1, r subcomponent. It has 102 of 117 bases (87%) identical to 1458-1574, 82 of 94 bases (87%) identical to 2052-2145, and 54 of 63 bases (85%) identical to 1678-1740 all fragments of *Homo sapiens* complement component 1, r subcomponent (GenBank Acc: NM_001733.1) (Table 5F).

Table 5F. BLASTN of FCTR5a against *Homo sapiens* complement component 1, r subcomponent (SEQ ID NO:79)

>GI|4502492|REF|NM_001733.1| HOMO SAPIENS COMPLEMENT COMPONENT 1, R SUBCOMPONENT (C1R), MRNA

LENGTH = 2386

SCORE = 113 BITS (57), EXPECT = 3E-22

IDENTITIES = 102/117 (87%)

STRAND = PLUS / PLUS

QUERY: 783 AGCCAAGCTGGGCAACTTCCCCTGGCAAGCCTTCACCAGTATCCACGGCCGTGGGGGCGG 842

[illegible]

SBJCT: 1458 AGCCAAGATGGGCAACTTCCCCTGGCAGGTGTTACCAACATCCACGGGCGCGGGGGCGG 1517

QUERY: 843 GGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCCACACCATCTACCCCAAGGA 899

|||||

SBJCT: 1518 GGCCCTGCTGGGCGACCGCTGGATCCTCACAGCTGCCACACCCTGTATCCCAAGGA 1574

SCORE = 91.7 BITS (46), EXPECT = 1E-15

IDENTITIES = 82/94 (87%)

STRAND = PLUS / PLUS

QUERY: 1380 CTGGGTGGCCACGGGCATTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTA 1439

|||||

SBJCT: 2052 CTGGGTGGCCACGGGCATCGTGTCCTGGGGCATCGGGTGCAGCAGGGGCTATGGCTTCTA 2111

QUERY: 1440 CACCAAGGTGCTCAGCTATGTGGACTGGATCAAG 1473

SBJCT: 2112 CACCAAAGTGCTCAACTACGTGGACTGGATCAAG 2145

SCORE = 54.0 BITS (27), EXPECT = 2E-04

IDENTITIES = 54/63 (85%)

STRAND = PLUS / PLUS

QUERY: 1006 CACCCCGACTACCGTCAGAATGAGTCCCATAACTTTAGCGGGGACATCGCCCTCCTGGAG 1065

[illegible]

SBJCT: 1678 CACCCGGACTACCGTCAGGATGAGTCCTACAATTTTGAGGGGGACATCGCCCTGCTGGAG 1737

QUERY: 1066 CTG 1068

1111

SBJCT: 1738 CTG 1740

The amino acid sequence of the protein of FCTR5a 485 of 487 amino acid residues (99%) identical to, and 487 of 487 residues (100%) positive with, the 487 amino acid complement C1r-like proteinase precursor from *Homo sapiens* (GenBank-ACC: AAF44349.1) (SEQ ID NO:80) (Table 5G).

Table 5G. BLASTP of FCTR5a and b against Complement C1R-like proteinase precursor (SEQ ID NO:80)

>GI|7706083|REF|NP_057630.1| COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
 GI|11436768|REF|XP_007061.1| COMPLEMENT C1R-LIKE PROTEINASE PRECURSOR, [HOMO SAPIENS]
 GI|7271475|GB|AAF44349.1|AF178985_1 (AF178985) COMPLEMENT C1R-LIKE PROTEINASE
 PRECURSOR [HOMO SAPIENS]
 LENGTH = 487

SCORE = 972 BITS (2513), EXPECT = 0.0
 IDENTITIES = 485/487 (99%), POSITIVES = 487/487 (100%)

R

QUERY: 1 MPGPRVWGKYLWRSPhSKGCPGAMWWLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1 MPGPRVWGKYLWRSPhSKGCPGAMWWLLWGVLQACPTRGSVLLAQELPQQLTSPGYPEP 60

QUERY: 61 YGKGQESSTDIAKEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQGSPLG 120
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 61 YGKGQESSTDIAKEGFAVRLVFQDFDLEPSQDCAGDSVTISFVGSDPSQFCGQGSPLG 120

QUERY: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 121 RPPGQREFVSSGRSLRLTFRTQPSSENKTAHLHKGFLALYQTVAVNYSQPISEASRGSEA 180

QUERY: 181 INAPGDNPAKVQNHQCPEPYQAAAAGALTCATPGTWKDRQDGEEVLQCMFVCGRPVTPIA 240
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 181 INAPGDNPAKVQNHQCPEPYQAAAAGALTCATPGTWKDRQDGEEVLQCMFVCGRPVTPIA 240

QUERY: 241 QNQTTLGSSRAKLGNFQWQAFSTIHGRGGGALLGDRWILTAAHTIYPKDSVSLRKNQSVN 300
 ||||||||||||||||||||||||||||||||||||||||||||||||||||+||||||
 SBJCT: 241 QNQTTLGSSRAKLGNFQWQAFSTIHGRGGGALLGDRWILTAAHTVYPKDSVSLRKNQSVN 300

QUERY: 301 VFLGHTAIDEMKLKGNHPVHRVVVHPDYRQNESHNFGDIALLELQHSIPLGPNVLPVCL 360
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 301 VFLGHTAIDEMKLKGNHPVHRVVVHPDYRQNESHNFGDIALLELQHSIPLGPNVLPVCL 360

QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTTELKYSRLPVAPREACNAWLQKRQRPVFSNMF 420
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTTELKYSRLPVAPREACNAWLQKRQRPVFSNMF 420

QUERY: 421 CVGDETQRHSVCQGDGSGSLYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
 ||||||||||||||||||||+||||||
 SBJCT: 421 CVGDETQRHSVCQGDGSGSVYVVWDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480

QUERY: 481 GVMNGKN 487
 |||||||
 SBJCT: 481 GVMNGKN 487

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY IS THE SAME.

The full amino acid sequence of the protein of FCTR5a has 175 of 303 amino acid residues (58%) identical to, and 226 of 303 residues (74%) positive with the 400-701 amino acid segment, 72 of 157 residues (45%) identical and 94 of 157 residues (59%) positive with amino acids 1-155, and 36 of 139 residues (25%) identical and 58 of 139 residues (40%) positive with amino acids 188-312 of the 705 amino acid Complement C1R Component Precursor from *Homo sapiens* (GenBank-ACC: AAA51851.1) (SEQ ID NO:43) (Table 5H).

Table 5H. BLASTP of FCTR5a and b against Complement C1R Component Precursor (SEQ ID NO:81)

5 >GI|115204|SP|P00736|C1R_HUMAN COMPLEMENT C1R COMPONENT PRECURSOR
GI|67614|PIR|C1HURB COMPLEMENT SUBCOMPONENT C1R (EC 3.4.21.41) PRECURSOR - HUMAN
GI|179644|GB|AAA51851.1| (M14058) HUMAN COMPLEMENT C1R [HOMO SAPIENS]
LENGTH = 705

SCORE = 361 BITS (928), EXPECT = 8E-99
IDENTITIES = 175/303 (58%), POSITIVES = 226/303 (74%), GAPS = 9/303 (2%)

QUERY: 189 AKVQNHQCPEYYQ-----AAAAGALTCATPGTWKDRQDGEEVLQCPMVCGRPVTPIA 240
 |++|+| |||+ | || | ||+ | ||++ +|+|||+| | +
 SBJCT: 400 ARIOYYCHPEYYKMOGRAGSRESEOGVYTCTAAGIWKNEOKGEKIPRCLPVCCKPVPNPVE 459

QUERY: 241 QNQTTLGSSRAKLGNFPWQAFTSIHGRGGGALLGDRWILTAHTIYPKDSVSLRKNQSVN 300
 | | + | + | + | | | | | | + | | | | | | | | | | | | | | + | | + + + | | ++
 SBJCT: 460 QRORIIGGOKAKMGNFPWQVFTNIHGRGGGALLGDRWILTAHTLYPKEHEA-QSNASLD 518

QUERY: 301 VFLGHTAIDEMCLKGNHPVHRVVVHPDYRQNESHNFSGDIALLELQHSIPLGPNVLPVCL 360
 ||||| ++|++|||||+ || |||||+||+| |||||++|+ |||+|+||
 SBJCT: 519 VFLGHTNVEELMKLGNHPIRRVSVHPDYRODESYNFEGDIALELENSVTLGPNLLPICL 578

QUERY: 361 PDNETLYRSGLLGYVSGFGMEMGWLTTTELKYSRLPVAPREACNAWLQKRQRPEVFSDNMF 420
 |||+| | ||+|||||+ + + ++ |||| +|| ||+ + | +|| |||
 SBJCT: 579 PDNDTFYDLGLMGYVSGFGVMEEKIAHDLRFVRLPVANPOACENWLRGKNRMDVFSQNMF 638

QUERY: 421 CVGDETQRHSCVCGDSSGLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIK 480
 | | + + ||||| ++ | | + ||||| ||||| || ||||| + |||||
 SBJCT: 639 CAGHPSLKQDACQDGGVFAVRDPNTDRWVATGIVSWGIGCSRGYGFYTKVLNLYVDWIK 698

QUERY: 481 GVM 483
|
SBJCT: 699 KEM 701

R
 QUERY: 24 MWLLLLWGVLAQCPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF 83
 ||| | | | | | + + + | ++|| | +|| | ++| | | | + +|||
 SBJCT: 1 MWLLYLLVPALEFCRAGGSIIPIKPLEGEVTSPLFPKYPNNEFTTTTIVTPTGYRVKLVF 60

QUERY: 84 QDFDLEPSQDCAGDSVTISFVGSQDPSQFCGQGSPLGRPPGQREFVSSGRSLRLTFRTPQ 143
 | | | | | + | | | | | + | | | | | | | | | + + | + | | + | | | |
 SBJCT: 61 QQFDLEPSECFYDYVKISADKKSLGRFCQQLGSPLGNPPGKKEFMSQGNKMLLTFTHTDF 120

```

QUERY: 144 SS-ENKTAHLHKGFALYQTVAVNYSQPISEASRGSE 179
          |+ || | + |||| || ||+ + | + ||
SBJCT: 121 SNEENGTFMFYKGFAYYO--AVDLDECASRSKSGEE 155

```

R
 QUERY: 35 ACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF-QDFDLEPSQD 93
 + | | | | ++ | | | + | + | + | | ++ |
 SBJCT: 188 SCAECSSSELYTEASGYISSLEYPRSYPPDLRCNYSIRVERGLTLHLKFLEPFDDIDHQQ 247

QUERY: 94 --CAGDSVTISFVGSDPSQFCGQGSPLGRPPGQREFVSSGRSLRLTFRTPQSSSENKTAH 151
 | | + | | + + ||| + + | ++ | | | ++
 SBJCT: 248 VHCOPYDOLOIYANGKNIGECFGKO-----RPP---DLDTSSNAVDLLFTTDES GDS----- 295

```

QUERY: 152 LHKGFLALYQTVAVNYSQP 170
          +|+  |  +  ||
SBJCT: 296 --RGWKLRYTTEIIKCPQP 312

```

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE HOMOLOGY IS THE SAME.

Based upon homology, FCTR5 proteins and each homologous protein or peptide may share at least some activity.

FCTR6

The novel nucleic acid of 1078 nucleotides FCTR6a (also designated 27455183.0.19) encoding a novel human blood coagulation factor XI-like protein is shown in Table 6A. An ORF was identified beginning with an ATG initiation codon at nucleotides 243-245 and ending with a TAA codon at nucleotides 1044-1046. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6A, and the start and stop codons are in bold letters.

Table 6A FCTR6a Nucleotide Sequence (SEQ ID NO:20)

TTGATCCGTCGCAAGTGGCTTTTGTGGGCTCTGTAGAGTGCTCTAAACCCAGCTCGGCCTTGTCTGTATTAGACAGAAGCACCTC
ATTCATATCCCTGGGGCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGCTATTCTGTTTTGTTTTGTTTTT
TCCTACCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGAGCTACATGGGATTTAGGTTTC
TGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCCTTCCACTTGGCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAA
CTGAGTGTCTGTCTGGGGACCAACGACTTAAGTAGCCCATCCATGGAAATAAAGGAGGTGCCAGCATCATCTTCACAAAGACTT
TAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCC
TCCCCACGCAGCCCCGGCCCTGCCACATGGCGCAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGCTGACAAAACTCTGTG
AAAACGGATCTGATGAAAGTGCCAATGGTTCATGAGTGGGAGGAGTGTCAAAGATGTTTCCAAACTTACCAAAAAATATGCT
GTGTGCCGATACAAGAATGAGAGCTATGATGCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCAGAGCCTGGTGAGA
AGTGGTACCAGGTGGGCATCATCAGCTGGGGAAGAGCTGTGGAGATAAGAACACCCAGGGATATACACCTCGTTGGTGAACCTAC
AACCTCTGGATCGAGAAAGTGACCCAGCTAGGAGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTAT
GGGCTCCCCAGTCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCATGTGTTGTCAGAG
CTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACCGAAA

The FCTR6a protein encoded by SEQ ID NO:20 has 267 amino acid residues and is presented using the one-letter code in Table 6B. FCTR6a was searched against other databases using SignalPep and PSort search protocols. The FCTR6a protein is most likely mitochondrial matrix space (Certainty= 0.4372) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR6a protein is 29412.8 daltons.

Table 6B. Encoded FCTR6a protein sequence (SEQ ID NO:21).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPPELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLASPIKLDDL
KVPICLPQTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPVIMDWEESCKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT
PEPGEKWYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS
HVLFRAILY

In an alternative embodiment, FCTR6b (alternatively referred to as 27455183.0.145) has the 1334 residue sequence shown in Table 6C. An ORF was identified beginning with an ATG initiation codon at nucleotides 499-501 and ending with a TAA codon at nucleotides 1300-1302. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6C, and the start and stop codons are in bold letters.

Table 6C FCTR6b Nucleotide Sequence (SEQ ID NO:22)

GATTTTAGAAGGTTAATCAAAACCGGGGACAGTTTCTTCATGGCATAACCAAGAGCTTGTGGCACCCTGCTG
CGTGGGATATCAATATCCTCTGGGGTTCGGAATGTGGGCTTATTACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTG
5 TAGACTAACTTCTGGTCTCTGAGTTTCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTAT
CTATCTGAAGGTGAGTTTGTATCCGTGCCAAGTGGCTTTTGTGGGCTGTGTAGAGTGTCTTAAACCCAGCTCGGCCTTTG
CTGTATTAGACAGAAGCACCTCATTATATCCCTGGGGCCCCTGATGGTGCAGTGGTCTGGCTGTGGTCTGCACACCAGC
TATTCTGTTTTGTTTTGTTTTGTTTTGTTTTCTACCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAG
GGTTTAAAGGTCTAGAGCTACATGGGATTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCC
10 TTCCACTTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCTGTCTGGGGACCAACGACTTAACTAGC
CCATCCATGGAAATAAAGGAGGTGCGCCAGCATCATTCTTCAAAAGACTTAAAGAGAGCCAACATGGACAATGACATTGC
CTTGCTGTCTGTGGCTTCGCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCA
CATGGCGGAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGTGACAAAACTCTGTGAAAACGGATCTGATGAAA
GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACCTACCAAAAATATGCTGTGTGCCGGATA
CAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCAGAGCCTGGTGAGAAGTGGT
15 ACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCAGGGATATACACCTCGTTGGTGAACATAC
AACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCAGGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAA
ACCTATGGGCTCCCCAGTCTCGGGAGTCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCTGTCCCATG
TGTTGTTCCAGAGCTATTTGTACTGATAATAAAATAGAGGCTATTCTTCAACCGAAA

The FCTR6b protein encoded by SEQ ID NO:22 has 267 amino acid residues and is presented using the one-letter code in Table 6B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the mitochondrial matrix space (Certainty=0.4372). The predicted molecular weight of this protein is 29498.9 Daltons.

Table 6D. Encoded FCTR6b protein sequence (SEQ ID NO:23).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPPEELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLASPIKLDDL
KVPICLPQTQPGPATWRECWVAGWGQTNAADKNSVKTDLMKVPVMIMDWEESCKMFPKLTKNMLCAGYKNESYDACKGDSGGPLVCT
PEPGEKWYQVGIIISWGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFNAEKRTSVKQKPMGSPVSGVPEPGSPRSWLLLCPLS
HVLFRAILY

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 853 of 897 bases (95 %) identical to bases 551-1447, and 346 of 388 bases (89%) identical to bases 127-513 of *Macaca fascicularis* brain cDNA, clone QccE-17034 (GENBANK-ID: |AB046651) (Table 6E).

Table 6E. BLASTN of FCTR6a against *Macaca fascicularis* brain cDNA, clone QccE-17034 (SEQ ID NO:82)

>GI|9651112|DBJ|AB046651.1|AB046651 MACACA FASCICULARIS BRAIN CDNA, CLONE QCCE-17034
LENGTH = 1746

SCORE = 1429 BITS (721), EXPECT = 0.0
IDENTITIES = 853/897 (95%)
STRAND = PLUS / PLUS

QUERY: 434 CCTTTTTCGAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCCTAGA 493
|||||
SBJCT: 551 CCTTTTTCGAATCCTCACACCTTCTGAGCTACAGCCCCAGTAGGGTCTAAATGTCCTAGA 610

QUERY: 494 GCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTC 553
|||||
SBJCT: 611 GCTATATGAGATTTAGGTTTCTGAGCACAGCCAATTCTCCCACTTTTGAGGCTTCCCTTC 670

QUERY: 554 CCCTTCCACTTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCTGTC 613
|||||

SBJCT: 671 CCCTTTCACTCGCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGTGTGAATGTCGTGC 730

QUERY: 614 TGGGGACCACTTAACTAGCCCATCCATGGAAATAAAGGAGGTGCCAGCATCATTC 673
|||||

SBJCT: 731 TGGGGACCAACGACTTAACTAGCTCATCCATGGAAATAAAGGAGGTGCCAGCATCATTC 790

QUERY: 674 TTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTT 733
|||||

SBJCT: 791 TTCACAAGGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCCT 850

QUERY: 734 CGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTG 793
|||||

SBJCT: 851 CGCCCATCACACTCGATGACCTGAAGGTGCCCATCTGCCTCCCTACGCAGCACGGCCCCG 910

QUERY: 794 CCACATGGCGGAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGCTGACAAAACT 853
|||||

SBJCT: 911 CCACATGGCACGAATGCTGGGTGGCAGGTGGGGCCAGACCAATGCTGCTGACAAAACT 970

QUERY: 854 CTGTGAAAACGGATCTGATGAAAGTGCCATGGTCATCATGGACTGGGAGGAGTGTTCAA 913
|||||

SBJCT: 971 CTGTGAAAACGGATCTGATGAAAGCGCCGATGGTCATCATGGACTGGGAGGAGTGTTCAA 1030

QUERY: 914 AGATGTTTCCAAAACCTACCAAAAATATGCTGTGTGCCGATACAAGAATGAGAGCTATG 973
||

SBJCT: 1031 AGGCGTTTCCAAAACCTACCAAAAATATGCTGTGTGCTGGATACAATAATGAGAGCTATG 1090

QUERY: 974 ATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1033
|||||

SBJCT: 1091 ACGCCTGCCAGGGTGACAGCGGGGGACCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1150

QUERY: 1034 GGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1093
|||||

SBJCT: 1151 GGTACCAGGTGGGTATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1210

QUERY: 1094 TATACACCTCGTTGGTGAACCTACAACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCA 1153
|||||

SBJCT: 1211 TATACACCTCGTTGGTGAACCTACAACCTCTGGATCGAGAAAGGTGACCCAGCTAGAGGGCA 1270

QUERY: 1154 GGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1213
|||||

SBJCT: 1271 GGCCCTTCAGTGCGGAGAAAATGAGGACCTCTGTCAAACAGAAACCTATGGGCTCCCGAG 1330

QUERY: 1214 TCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1273
|||||

SBJCT: 1331 TCTCGGGGGTCCCAGAGCCAGGCGGCCCTCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1390

QUERY: 1274 ATGTGTTGTTTCAGAGCTATTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACC 1330
|||||

SBJCT: 1391 ATGTGTTGTTTCAGAGCTATTTGTACTGATAATAAAATAGAGGCTATTTTTCATCAACC 1447

SCORE = 428 BITS (216), EXPECT = E-117
IDENTITIES = 346/388 (89%), GAPS = 1/388 (0%)
STRAND = PLUS / PLUS

```

QUERY: 1      GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCT 60
              |||
SBJCT: 127     GATTTTAGAAGGTTAATCAAAAACCCAAGGACAGTTTTCATCATGTCAATAACCAAAGACCC 186
              |||
QUERY: 61      TTGTGGCACCCGCTGTCTGTTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTAT 120
              |||
SBJCT: 187     TTGTGGCACCTGCTGTCTCATGGGATAACAAATATCTTGTGGGGTTCGGAATGTGGACTTAT 246
              |||
QUERY: 121     TACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTCTAGACTAACTTCTGGTCCTGAGTT 180
              |||
SBJCT: 247     TACTGAAGCTCCTGTCTGCTTGGTCAGTGG-TGGTCTAGACTAACTTCTGGTCCTGAGAT 305
              |||
QUERY: 181     TCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTATCTAT 240
              |||
SBJCT: 306     TCTAAAGTGTTGGTAGACCGGTTGAGATAAAAGATATATAATAATGAATGCCTTACCTAT 365
              |||
QUERY: 241     CTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAA 300
              |||

```

[illegible]

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 295 of 378 bases (78 %) identical to bases 410-779 of *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (GENBANK-ID:AK09660) (Table 6F).

Table 6F. BLASTN of FCTR6a against *Mus musculus* adult male testis cDNA, RIKEN full-length enriched (SEQ ID NO:83)

>GI|12855429|DBJ|AK016601.1|AK016601 MUS MUSCULUS ADULT MALE TESTIS CDNA, RIKEN FULL-LENGTH ENRICHED

LIBRARY, CLONE:4933401F05, FULL INSERT SEQUENCE
LENGTH = 1047

SCORE = 97.6 BITS (49), EXPECT = 2E-17
IDENTITIES = 295/378 (78%), GAPS = 8/378 (2%)
STRAND = PLUS / PLUS

QUERY: 697 AACATGGACAATGACATTGCCTTGCTGCTGGCTTCGCCCATCAAGCTCGATGACCTG 756

SBJCT: 410 AACATGGACAACGACATTGCCTTGTTGCTGCTAGCCAAGCCCTTGACGTTCAATGAGCTG 469

QUERY: 757 AAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCACATGGCGCAATGCTGGGTG 816

SBJCT: 470 ACGGTGCCCATCTGCCTTCCTCTCTGGCCCGCCCTCCCAGCTGGCACGAATGCTGGGTG 529

OUERY: 817 GCAGGTTGGGGCCAGACCAATGCTGCTGACAAAACTCTGTGAAAACGGATCTGATGAAA 876

||||| ||||| ||||| | ||||| ||||| ||||| ||||| ||||| |||||
SBJCT: 530 GCAGGATGGGGCGTAACCAACTCAACTGACAAGGAATCTATGTCAACGGATCTGATGAAG 589

OUERY: 877 GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCCAAAACCTTACCAA 936

SBJCT: 590 GTGCCCATGCGTATCATAGAGTGGGAGGAATGCTTACAGATGTTTCCCAGCCTCACCACA 649

OUERY: 937 AATATGCTGTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGG 996

SBJCT: 650 AACATGCTGTGTGCCTCATATGGTAATGAGAGCTACGATGCTTGC-----CAGTGGG 701

QUERY: 997 GGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGTGGTACCAGGTGGGCATCATCAGC 1056

SBJCT: 702 GGACCGCTTTGTCTGCACCAAGATCCTGGCAGTAGGTGGTACCAGGTGGGCATCATCAGC 761

QUERY: 1057 TGGGGAAAGAGCTGTGGA 1074

SBJCT: 762 TGGGGCAAGAGCTGTGGA 779

The FCTR6a amino acid has 247 of 267 amino acid residues (92%) identical to, and 251 of 307 residues (94%) positive with, the 267 amino acid hypothetical protein [*Macaca fascicularis*] (GenBank: AB046651) (SEQ ID NO:84) (Table 6G).

SBJCT: 548 CQKRYQDYK MFCAGYKEGGKDGSGGPLVC--KHNGMWR TSWGEGCARR 605

QUERY: 195 NTPGIYTSLVNYNLWIEKVQ 215

SBJCT: 606 EQPGVYTKVAEYMDWILEKTQ 626

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 73 of 183 amino acid residues (39%) identical to, and 110 of 183 residues (59%) positive with, the 643 amino acid kallikrein [*Sus scrofa*] (GENBANK-ID:BAA37147.1) (SEQ ID NO:86) (Table 6I).

Table 6I. BLASTP of FCTR6a and b against kallikrein [*Sus scrofa*] (SEQ ID NO:86)

>GI|4165315|DBJ|BAA37147.1| (AB022425) KALLIKREIN [SUS SCROFA]
LENGTH = 643

SCORE = 128 BITS (322), EXPECT = 9E-29
IDENTITIES = 73/183 (39%), POSITIVES = 110/183 (59%), GAPS = 12/183 (6%)

QUERY: 38 VLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLASPIKLDLKVPICLPTQ 95
+| +++| +| ++|| |||+++| +|||| | +| + | + ||||++
SBJCT: 459 ILNISEITKETPFQSQVKE---IIHQNYKILESGHDIALLKLETPLNYTDFQKPICLPSR 515

QUERY: 96 PGP-ATWRECWVAGWGQTNAADKNSVKTDLMKVPVIMDWEESKMF--KLTKNMLCAG 152
+ ||| ||| | +| ++ | || + ++ ||| | + |++| |++||
SBJCT: 516 DDTNVVYTNCWVTGWGFTE--EKGEIQNILQKVNIPVSNBECQKSYRDHKISKQMICAG 573

QUERY: 153 YKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEK 212
|| |||||+||||||| + +| + ||| + | + |||| ++ | || +
SBJCT: 574 YKEGGKDGSGGPLVC--KYNGIWHLVGTTSWGEGCARREQPGVYTKVIEYMDWILE 631

QUERY: 213 VTQ 215

SBJCT: 632 KTQ 634

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 81 of 205 amino acid residues (39%) identical to, and 112 of 205 residues (54%) positive with, the 625 amino acid Coagulation factor XI [*Homo sapiens*] (embCAA64368.1) (SEQ ID NO:87) (Table 6J).

Table 6J. BLASTP of FCTR6a and b against Coagulation factor XI [*Homo sapiens*] (SEQ ID NO:87)

>GI|180352|GB|AAAS1985.1| (M20218) COAGULATION FACTOR XI [HOMO SAPIENS]
LENGTH = 625

SCORE = 127 BITS (320), EXPECT = 1E-28
IDENTITIES = 81/205 (39%), POSITIVES = 112/205 (54%), GAPS = 17/205 (8%)

QUERY: 20 LPLAPLWFSATSPHEELSVVLGTNDLTSPSMEIKE-----VASIILHKDFKRANMDNDIA 73
| | ++ ||+ | | | + + |||| | ||+ +| | |||
SBJCT: 427 LTAHCFYGVESPKILRVYSGILNQS----EIKEDTSFFGVQEIIHDQYKMAESGYDIA 482

QUERY: 74 LLLLASPIKLDLKVPICLPTQPG-PATWRECWVAGWGQTNAADKNSVKTDLMKVPVIM 132
|| | + + | + |||||++ + +||| ||| || ++ | | + ++
SBJCT: 483 LLKLETTVNYTDSQRPICLPSKGDNRVIYTDWCWVTGWGYRKLKRDK--IQNTLQKAKIPLV 540

QUERY: 133 DWEESKMF--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKS 190

||| | + | + | + ||| + ||| ||| ||| + | + ||| ||| +
 SBJCT: 541 TNEECQKRYE THKMICAGYREGGKDACKGDSGGPLSC--KHN LVGITSWGEG 598
 K
 QUERY: 191 CGDKNTPGIYTSLVNLYNLWIEKVTQ 215
 | + ||| + | | + ||
 SBJCT: 599 CAQRERPGVYTNVVEYVDWILEKTQ 623

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The number of new cases of renal cell carcinoma in the United States in 1996 was projected to be 30,600 with an estimated 12,000 deaths. Tumors with a proposed histogenesis from the proximal tubule (clear-cell and chromophilic tumors) amount to 85% of renal cancers, whereas tumors with a proposed histogenesis from the connecting tubule/collecting duct (chromophobic-, oncocytic-, and duct Bellini-type tumors) amount to only 11%.

Adenocarcinomas may be separated into clear cell and granular cell carcinomas, although the 2 cell types may occur together in some tumors. The distinction between well-differentiated renal carcinomas and renal adenomas can be difficult. The diagnosis is usually made arbitrarily on the basis of size of the mass, but size alone should not influence the treatment approach, since metastases can occur with lesions as small as 0.5 centimeters.

While radical nephrectomy with regional lymphadenectomy, is the accepted, often curative therapy for stage I (localized disease) renal cell cancer, very little therapy is available for advance disease that represent about 70% of the patients. Radiotherapy as a postoperative adjuvant has not been effective, and when used preoperatively, may decrease local recurrence but does not appear to improve 5-yr survival. A chemotherapeutic agent capable of significantly altering the course of metastatic renal cell carcinoma has not been identified. (Renal Cell Cancer (PDQ®) Treatment - Health Professionals, Cancernet, NCI)

There is therefore a need to identify genes that are differentially modulated in renal-cell carcinomas. In addition there is a need for methods to assay candidate therapeutic substances for modulating expression of these genes. These substances might be recombinant protein expressed by the identified genes or antibodies that bind to the identified proteins. There is yet additionally a need for an effective method of identifying target molecules or related components. These and related needs and defects are addressed in the present invention.

Novel kallikrein-like/coagulation factor XI-like Proteins and Nucleic Acids Encoding Same

FCTR6 is surprisingly found to be differentially expressed in clear cell Renal cell carcinoma tissues vs the normal adjacent kidney tissues. The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to kallikrein-like, nucleic acids that encode these proteins or

fragments thereof, and antibodies that bind immunospecifically to protein of the invention. It may have use as a therapeutic agent in the treatment of renal cancer and liver cirrhosis.

The utility of kallikrein family members in protein therapy of Renal cancer

The treatment of renal cell carcinoma with recombinant kallikrein could improve disease outcome through several potential mechanisms. The literature suggests that members of this protein family are inhibitory to the process of angiogenesis, a process of vital importance to tumor progression. Renal cell carcinoma is known to be a highly angiogenic cancer. Thus, treatment of renal cell carcinoma with kallikrein may effectively shutdown the active recruitment of a blood supply to a tumor. Members of this protein family are known to play a role in vascular coagulation. Similar to anti-angiogenic therapy, a factor produced by cancer cells that is pro-coagulatory may also act to inhibit cancer growth by effectively "clogging" the tumor vascular supply. In addition, through its proteolytic activity, kallikrein may degrade ECM proteins or growth factors necessary for the progressive growth of cancer cells. Following is a relevant reference underlining the importance of Kallikrein in cancer therapy.

The New Human Kallikrein Gene Family: Implications in Carcinogenesis.

Diamandis EP; Yousef GM; Luo I; Magklara I; Obiezu CV

Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada.

Trends Endocrinol Metab 2000 Mar;11(2):54-60.

ABSTRACT: The traditional human kallikrein gene family consists of three genes, namely KLK1 [encoding human kallikrein 1 (hK1) or pancreatic/renal kallikrein], KLK2 (encoding hK2, previously known as human glandular kallikrein 1) and KLK3 [encoding hK3 or prostate-specific antigen (PSA)]. KLK2 and KLK3 have important applications in prostate cancer diagnostics and, more recently, in breast cancer diagnostics. During

the past two to three years, new putative members of the human kallikrein gene family have been identified, including the PRSSL1 gene [encoding normal epithelial cell-specific 1 gene (NES1)], the gene encoding zyme/protease M/neurosin, the gene encoding prostase/KLK-L1, and the genes encoding neuropsin, stratum corneum chymotryptic enzyme and trypsin-like serine protease. Another five putative kallikrein genes, provisionally named KLK-L2, KLK-L3, KLK-L4, KLK-L5 and KLK-L6, have also been identified. Many of the newly identified kallikrein-like genes are regulated by steroid hormones, and a few kallikreins (NES1, protease M, PSA) are known to be downregulated in breast and possibly other cancers. NES1 appears to

be a novel breast cancer tumor suppressor protein and PSA a potential inhibitor of angiogenesis. This brief review summarizes recent developments and possible applications of the newly defined and expanded human kallikrein gene locus.

The utility of kallikrein-like/coagulation factor XI-like family members in protein therapy of liver cirrhosis

Results related to inflammation shown below in Example A, Table CC3, panel 4, indicate over-expression of 27455183.0.19 in the liver cirrhosis sample, as compared to panel 1 data (Table CC1), where there is little or no expression in normal adult liver. Panel 4 was generated from various human cell lines that were untreated or resting as well as the same cells that were treated with a wide variety of immune modulatory molecules. There are several disease tissues represented as well as organ controls.

Potential Role(s) of FCTR6 in Inflammation:

Liver cirrhosis occurs in patients with hepatitis C and also in alcoholics. This protein is 41% related to coagulation factor XI and its potential role in liver cirrhosis may be related to cleavage of kininogen. A reference for this follows:

Thromb Haemost 2000 May;83(5):709-14 High molecular weight kininogen is cleaved by FXIa at three sites: Arg409-Arg410, Lys502-Thr503 and Lys325-Lys326. Mauron T, Lammle B, Wuillemin WA Central Hematology Laboratory, University of Bern, Inselspital, Switzerland. Abstract:

We investigated the cleavage of high molecular weight kininogen (HK) by activated coagulation factor XI (FXIa) in vitro. Incubation of HK with FXIa resulted in the generation of cleavage products which were subjected to SDS-Page and analyzed by silverstaining, ligand-blotting and immunoblotting, respectively. Upon incubation with FXIa, bands were generated at 111, 100, 88 kDa on nonreduced and at 76, 62 and 51 kDa on reduced gels. Amino acid sequence analysis of the reaction mixtures revealed three cleavage sites at Arg409-Arg410, at Lys502-Thr503 and at Lys325-Lys326. Analysis of HK-samples incubated with FXIa for 3 min, 10 min and 120 min indicated HK to be cleaved first at Arg409-Arg410, followed by cleavage at Lys502-Thr503 and then at Lys325-Lys326. In conclusion, HK is cleaved by FXIa at three sites. Cleavage of HK by FXIa results in the loss of the surface binding site of HK, which may constitute a mechanism of inactivation of HK and of control of contact system activation.

Impact of Therapeutic Targeting of FCTR6 in Inflammation:

Therapeutic targeting of FCTR6 with a monoclonal antibody is anticipated to limit or block the extent of breakdown of kininogen and thereby reduce the degradation of liver that occurs in liver cirrhosis. A pertinent reference is:

Thromb Haemost 1999 Nov;82(5):1428-32 Parallel reduction of plasma levels of high and low molecular weight kininogen in patients with cirrhosis.

Cugno M, Scott CF, Salerno F, Lorenzano E, Muller-Esterl W, Agostoni A, Colman RW
Department of Internal Medicine, IRCCS Maggiore Hospital, University of Milan, Italy.
massimo.cugno@unimi.it

Abstract:

Little is known about the regulation of high-molecular-weight-kininogen (HK) and low-molecular-weight-kininogen (LK) or the relationship of each to the degree of liver function impairment in patients with cirrhosis. In this study, we evaluated HK and LK quantitatively by a recently described particle concentration fluorescence immunoassay (PCFIA) and qualitatively by SDS PAGE and immunoblotting analyses in plasma from 33 patients with cirrhosis presenting various degrees of impairment of liver function. Thirty-three healthy subjects served as normal controls. Patients with cirrhosis had significantly lower plasma levels of HK (median 49 microg/ml [range 22-99 microg/ml]) and LK (58 microg/ml [15-100 microg/ml]) than normal subjects (HK 83 microg/ml [65-115 microg/ml]; LK 80 microg/ml [45-120 microg/ml]) ($p < 0.0001$). The plasma concentrations of HK and LK were directly related to plasma levels of cholinesterase ($P < 0.0001$) and albumin ($P < 0.0001$ and $P < 0.001$) and inversely to the Child-Pugh score ($P < 0.0001$) and to prothrombin time ratio ($P < 0.0001$) (reflecting the clinical and laboratory abnormalities in liver disease). Similar to normal individuals, in patients with cirrhosis, plasma HK and LK levels paralleled one another, suggesting that a coordinate regulation of those proteins persists in liver disease. SDS PAGE and immunoblotting analyses of kininogens in cirrhotic plasma showed a pattern similar to that observed in normal controls for LK (a single band at 66 kDa) with some lower molecular weight forms noted in cirrhotic plasma. A slight increase of cleavage of HK (a major band at 130 kDa and a faint but increased band at 107 kDa) was evident. The increased cleavage of HK was confirmed by the lower cleaved kininogen index (CKI), as compared to normal controls. These data suggest a defect in hepatic synthesis as well as increased destructive cleavage of both kininogens in plasma from patients with cirrhosis. The decrease of important regulatory proteins like kininogens may contribute to the imbalance in coagulation and fibrinolytic systems, which frequently occurs in cirrhotic patients.

In summary, the differential expression of FCTR6 (Kallikrein family) in renal cell carcinoma is an important finding that could have immense potential in renal carcinogenesis. In

additon, overexpression of the above gene in liver cirrhosis demonstrates its anticipated use as an immunotherapeutic target

FCTR7

The novel nucleic acid of 1498 nucleotides FCTR7 (also designated. 32592466.0.64) encoding a novel trypsin inhibitor-like protein is shown in Table 7A. An ORF begins with an ATG initiation codon at nucleotides 470-472 and ends with a TAA codon at nucleotides 1369-1371. Putative untranslated regions, if any, are found upstream from the initiation codon and downstream from the termination codon.

Table 7A. FCTR7 Nucleotide Sequence (SEQ ID NO:24)

AGGCGCCTGGTTCTGCGCTACTGGCTGTACGGAGCAGGAGCAAGAGGTCGCGCCAGCCTCCGCGCCGAGCCTCGTTTCGTGTCC
CGCCCCCTCGCTCCTGCAGCTACTGCTCAGAAACGCTGGGGCGCCACCCTGGCAGACTAACGAAGCAGCTCCCTTCCCACCCCAA
CTGCAGGTCTAATTTTGGACGCTTTGCCCTGCCATTTCTTCCAGGTTGAGGGAGCCGCAGAGGCGGAGGCTCGCGTATTCTGCAGT
CAGCACCACGTCGCCCCCGGACGCTCGGTGCTCAGGCCCTTCGCGAGCGGGGCTCTCCGTCTGCGGTCCCTTGTAAGGCTCTGG
GCGGCTGCAGAGGCCGGCCGTCGCGTTTGGCTCACCTCTCCAGGAACTTCACACTGGAGAGCCAAAAGGAGTGGAAGAGCCTGT
CTTGGAGATTTCTGCGGAAATCCTGAGGTCATTATTATGAAGTGTACCGCGCGGAGTGCGTCAGAGTAACCACAGTGCTGTT
CATGGCTAGAGCAATTCAGCCATGGTGGTTCCTCAATGCCACTTTATTGGAGAACTTTTGAAAAATACATGGATGAGGATGGTG
AGTGGTGGATAGCCAAACAACGAGGGAAAAGGGCCATCACAGACAATGACATGCAGAGTATTTGGACCTTCATAATAAATTACGA
AGTCAGGTGTATCCAACAGCCTCTAATATGGAGTATATGACATGGGATGTAGAGCTGGAAAGATCTGCAGAATCCAGGGCTGAAAT
TGCTTGTGGGAACATGGACCTGCAAGCTTGCTTCCATCAATTGGACAGAATTTGGGAGCACACTGGGGAAGATATAGGCCCCGAC
GTTTCATGTACAATCGTGGTATGATGAAGTGAAGACTTTAGCTACCCATATGAACATGAATGCAACCCATATTGTCCATTGAGGT
GTTCTGGCCCTGTATGTACACATTATACACAGGTCGTGTGGGCAACTAGTAACAGAATCGGTTGTGCCATTAATTTGTGTCTAAC
ATGAACATCTGGGGGAGATATGGCCCAAAGCTGTCTACCTGGTGTGCAATTACTCCCCAAAGGGAACTGGTGGGGCCATGCCCC
TTACAAACATGGGCGGCCCTGTTCTGCTTGCCACCTAGTTTGGAGGGGGCTGTAGAGAAAATCTGTGTACAAAGAAGGGTCAG
ACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATGAAATAGAACGGCAGCAGTCACAAGTCCATGACACCCATGTCCGGACAAGA
TCAGATGATAGTAGCAGAAATGAAGTCATTAGCTTTGGGAAAAGTAATGAAAATATAATGGTTTTAGAAATCCTGTGTTAAATATT
GCTATATTTCTTAGCAGTTATTTCTACAGTTAATTACATAGTCATGATTGTTCTACGTTTCATATATTATATGGTGCTTTGTATA
TGCCCCCTAATAAAATGAATCTAAACATTGAAAAAA

The FCTR7 protein encoded by SEQ ID NO:24 has 300 amino acid residues and is presented using the one-letter code in Table 7B. The FCTR7 gene was found to be expressed in: brain; germ cell tumors. FCTR7 gene maps to Unigene cluster Hs.182364 which is expressed in the following tissues: brain, breast, ear, germ cell, heart, liver, lung, whole embryo, ovary, pancreas, pooled, prostate, stomach, testis, uterus, vascular. Therefore the FCTR7 protein described in this invention is also expressed in the above tissues.

The SignalP, Psort and/or Hydropathy profile for FCTR7 predict that this sequence has a signal peptide and is likely to be localized outside of the cell with a certainty of 0.4228. The SignalP shows a cleavage site between amino acids 20 and 21, *i.e.*, at the dash in the sequence amino acid ARA-IP. The predicted molecular weight of FCTR7 is 34739.9 Daltons. Hydropathy profile shows an amino terminal hydrophobic region. This region could function as a signal peptide and target the invention to be secreted or plasma membrane localized.

Table 7B. Encoded FCTR7 protein sequence (SEQ ID NO:25).

MKCTAREWLRVTTVLFMARAI...VVPNATLLEKLLKYMDEDEGEWWIAKQRGKRAIT...ADMQSILDLHNKLR SQVYPTASNMEYM
TWDVELERSAESRAESCLWEHGPA SLLPSIGQNLGAHWGRYPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVV
WATSNRIGCAINLCHNMNIWGQIWPKAVYLV CNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENL CYKEGSDRYYP PREEETNE
IERQQSQVHDTHVRTRSDSSRNEVISFGKSNENIMVLEILC

This gene maps to Unigene cluster Hs.182364 which has been assigned the following mapping information shown in table 7C. Therefore the chromosomal assignment for this gene is the same as that for Unigene cluster 182364.

Table 7C. Mapping Information.

Chromosome: 8
Gene Map 98: Marker SHGC-32056 , Interval D8S279-D8S526
Gene Map 98: Marker SGC32056 , Interval D8S526-D8S275
Gene Map 98: Marker sts-G20223 , Interval D8S526-D8S275
Gene Map 98: Marker stSG30385 , Interval D8S526-D8S275
Whitehead map: EST67946, Chr.8
dbSTS entries: G25853, G29349, G20223

The predicted amino acid sequence was searched in the publicly available GenBank database

FCTR7 protein showed Score = 743 (261.5 bits), Expect = 1.4e-73, P = 1.4e-73, 54 % identities (129 over 237 amino acids) and 43% homologies (167 over 237 amino acids) with human 25 kD trypsin inhibitor protein (258 aa; ACC:O43692) (Table 7D).

Table 7D. BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - HO... +2 743 8.4e-73 1 (SEQ ID NO:88)
ptnr:SPTREMBL-ACC:O44228 HRTT-1 - HALOCYNTHIA RORETZI ... +2 325 2.9e-28 1 (SEQ ID NO:89)
ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED ... +2 314 5.3e-27 1 (SEQ ID NO:90)
ptnr:PIR-ID:JC4131 glioma pathogenesis-related protein... +2 309 2.0e-26 1 (SEQ ID NO:91)
ptnr:SWISSNEW-ACC:O19010 CYSTEINE-RICH SECRETORY PROTE... +2 258 9.4e-21 1 (SEQ ID NO:92)

The nucleotide sequence of FCTR7 has 954 of 957 residues (99 %) identical to the 1-957 base segment, and 174 of 175 residues (99%) identical to bases 1317-1953 of the 2664

nucleotide *Homo sapiens* putative secretory protein precursor, mRNA (GenBank-ACC: AF142573) (SEQ ID NO. 93) (Table 7E).

Table 7E. BLASTN of FCTR7 against Putative secretory protein precursor (SEQ ID NO:93)

5 >gi|12002310|qb|AF142573.1|AF142573 Homo sapiens putative secretory protein precursor, mRNA, complete cds
Length = 2664

Score = 1865 bits (941), Expect = 0.0
Identities = 954/957 (99%), Gaps = 1/957 (0%)
Strand = Plus / Plus

10 Query: 364 gtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 423
Sbjct: 1 gtccggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 60

Query: 424 agcctgtcttggagattttctctggggaaatcctgaggtcattcattatgaagtgtaccgc 483
Sbjct: 61 agcctgtcttggagattttctctggggaaatcctgaggtcattcattatgaagtgtaccgc 120

20 Query: 484 gcgggagtggtcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 543
Sbjct: 121 gcgggagtggtcagagtaaccacagtgctgttcatggctagagcaattccagccatggt 180

25 Query: 544 ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 603
Sbjct: 181 ggttcccaatgccactttattggagaaacttttggaaaaatacatggatgaggatggtga 240

30 Query: 604 gtggtggatagccaaacaacgaggggaaaagggccatcacagacaatgacatgcagagtat 663
Sbjct: 241 gtggtggatagccaaacaacgaggggaaaagggccatcacagacaatgacatgcagagtat 300

35 Query: 664 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 723
Sbjct: 301 tttggaccttcataataaattacgaagtcaggtgtatccaacagcctctaatatggagta 360

40 Query: 724 tatgacatgggatgtagagctggaaagatctgcagaatccagggctgaaa-ttgcttggtg 782
Sbjct: 361 tatgacatgggatgtagagctggaaagatctgcagaatcctgggctgaaagttgcttggtg 420

45 Query: 783 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 842
Sbjct: 421 ggaacatggacctgcaagcttgcttccatcaattggacagaatttgggagcacactgggg 480

50 Query: 843 aagatataggcccccgacgtttcatgtacaatcgtgggtatgatgaagtgaagacttttag 902
Sbjct: 481 aagatataggcccccgacgtttcatgtacaatcgtgggtatgatgaagtgaagacttttag 540

55 Query: 903 ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 962
Sbjct: 541 ctacccatatgaacatgaatgcaacccatattgtccattcaggtgttctggccctgtatg 600

Query: 963 tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttggtgccattaattt 1022
Sbjct: 601 tacacattatacacaggtcgtgtgggcaactagtaacagaatcggttggtgccattaattt 660

Query: 1023 gtgtcataacatgaacatctgggggagatatggcccaaagctgtctacctggtgtgcaa 1082
Sbjct: 661 gtgtcataacatgaacatctgggggagatatggcccaaagctgtctacctggtgtgcaa 720

Query: 1083 ttactc...aagggaaactggtggggccatgcccctta...acatgggcggccctgttc 1142
 Sbjct: 721 ttactccccaagggaaactggtggggccatgccccttacaaacatgggcggccctgttc 780

Query: 1143 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc 1202
 Sbjct: 781 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc 840

Query: 1203 agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca 1262
 Sbjct: 841 agacaggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca 900

Query: 1263 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 1319
 Sbjct: 901 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 957

Score = 339 bits (171), Expect = 3e-90
 Identities = 174/175 (99%)
 Strand = Plus / Plus

Query: 1317 cattagctttgggaaaagtaatgaaaatataatggtttttagaaatcctgtgttaaatt 1376
 Sbjct: 1779 cattagctttgggaaaagtaatgaaaatataatggtttttagaaatcctgtgttaaatt 1838

Query: 1377 gctatattttcttagcagttatttctacagttaattacatagtcattgttctacgtt 1436
 Sbjct: 1839 gctatattttcttagcagttatttctacagttaattacatagtcattgttctacgtt 1898

Query: 1437 tcataattatatggtgctttgtatatgcccctaataaaaatgaatctaaacattg 1491
 Sbjct: 1899 tcataattatatggtgctttgtatatgcccctaataaaaatgaatctaaacattg 1953

The FCTR7 amino acid has 284 of 285 amino acid residues (99%) identical to, and 284 of 285 amino acid residues (99%) similar to, the 500 amino acid Putative secretory protein precursor [*Homo sapiens*] (GenBank-Acc No.: AF142573) (SEQ ID NO:94) (Table 7F).

Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor, (SEQ ID NO:94)

>gi|12002311|qb|AAG43287.1|AF142573_1 (AF142573) putative secretory protein precursor [*Homo sapiens*]
 Length = 500

Score = 581 bits (1499), Expect = e-165
 Identities = 284/285 (99%), Positives = 284/285 (99%)

Query: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDEGEWWIAKQRGKRAITDN 60
 Sbjct: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDEGEWWIAKQRGKRAITDN 60

Query: 61 DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIQNL 120
 Sbjct: 61 DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESWAESCLWEHGPASLLPSIQNL 120

Query: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWATSNRIG 180
 Sbjct: 121 GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWATSNRIG 180

Query: 181 CAINLCHNMNIWGQIWPKAVYLV CNYS PKGNWGWGHAPYKHGRPCSACPPSF GGGCRENL C 240

Sbjct: 181 CAINLCHWGQIWPKAVYLVNYSKGNWGHAPYKH SACPPSFGGGCRENLC 240
 Query: 241 YKEGSDRYPPREEETNEIERQQSQVHDTHVTRSDSSRNEVIS 285
 Sbjct: 241 YKEGSDRYPPREEETNEIERQQSQVHDTHVTRSDSSRNEVIS 285

The FCTR7 amino acid has 137 of 176 amino acid residues (78%) identical to, and 151 of 176 amino acid residues (86%) similar to, the 188 amino acid Late gestation lung protein 1 [*Rattus norvegicus*] (GenBank-Acc No.: AF109674) (SEQ ID NO:95) (Table 7G).

Table 7G. BLASTP alignments of FCTR7 against Late gestation lung protein 1, (SEQ ID NO:95)

>gi|4324682|gb|AAD16986.1| (AF109674) late gestation lung protein 1 [*Rattus norvegicus*]

Length = 188

Score = 277 bits (709), Expect = 1e-73

Identities = 137/176 (78%), Positives = 151/176 (86%)

Query: 68 LHNKLRQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRY 127
 Sbjct: 2 LHNKLRGQVYPPASNMEYMTWDEELERSAAAWAQRCLWEHGPASLLVSIGQNLAVHWGRY 61
 Query: 128 RPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVWVWATSNRIGCAINLCH 187
 Sbjct: 62 RSPGFHVQSWYDEVKDYTPYPHECNPWCPERC SGAMCTHYTQMWWATTNKIGCAVHTCR 121
 Query: 188 NMNIWGQIWPKAVYLVNYSKGNWGHAPYKHGRPCSACPPSFGGGCRENLCYKE 243
 Sbjct: 122 SMSVWGDIWENAVYLVNYSKGNWIGEAPYKHGRPCSECPSSYGGGCRNNLCYRE 177

The FCTR7 amino acid has 130 of 237 amino acid residues (55%) identical to, and 165 of 237 amino acid residues (70%) similar to, the 258 amino acid R3H domain-containing preproprotein; 25 kDa trypsin inhibitor [*Homo sapiens*] (GenBank-Acc No.: D45027) (SEQ ID NO:96) (Table 7H).

Table 7H. BLASTP alignments of FCTR7 against R3H domain-containing preproprotein, 25 kDa trypsin inhibitor (SEQ ID NO:96)

>gi|7705676|ref|NP_056970.1| R3H domain-containing preproprotein; 25 kDa trypsin inhibitor; R3H domain (binds single-stranded nucleic acids) containing [*Homo sapiens*]
 gi|2943716|dbj|BAA25066.1| (D45027) 25 kDa trypsin inhibitor [*Homo sapiens*]
 Length = 258

Score = 265 bits (678), Expect = 4e-70

Identities = 130/237 (55%), Positives = 165/237 (70%), Gaps = 3/237 (1%)

Query: 12 TTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWIIAKQRGKRAITDNDMQSILDLHNK 71
 Sbjct: 20 STVVLNSTDSSPPTNFTDIEAALKAQLDSAD---IPKARRKRYISQNDMIAILDYHNQ 76

```

Query: 72  LRSQVYPTASNM EYMTWDV ELERSAESRAESCLWEHG PASILRSIGQNLGAHWGRYRPPT 131
          +| +|+| ● |||| | | | ||| | | +|+|++ ● +||| |||
Sbjct: 77  VRGKVFPP ● ENMEYMVWDENLAKSAEAWAATCIWDHG PSYLLRFLGQNL SVRTGRYRSIL 136

Query: 132  FHVQSWYDEVKDFSYPYEH ECNPYCPFRCSGPVCTHYTQV VWATSNRIGCAINLCHNMNI 191
          | + ||||| |+++| | +|| | | | | +||| | +||| | | | + | ||| +
Sbjct: 137  QLVKPYWDEVKDYAFPPYQDCNPRCPMRCFGPMCTHYTQM VWATSNRIGCAIHTCQNMNV 196

Query: 192  WGQIWPKAVYLV CNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENL CYKEGSDRY 248
          || +| +| ||||| | +||| | | ||| | | +||| +|| | +||| + |
Sbjct: 197  WGSVWRRAYLV CNYAPKGNWIGEAPYKVGVPSCSPPSYGGSCDNL CFPGVTSNY 253

```

The FCTR7 amino acid has 109 of 233 amino acid residues (47%) identical to, and 146 of 233 amino acid residues (63%) similar to, the 253 amino acid Novel protein similar to a trypsin inhibitor [*Homo sapiens*] 25 kDa trypsin inhibitor (EMBLAcc No.: AL117382) (SEQ ID NO:97) (Table 7I).

Table 7I. BLASTP alignments of FCTR7 against Novel protein similar to a trypsin inhibitor, (SEQ ID NO:97)

```
>gi|9885193|emb|CAC04190.1| (AL117382) dJ881L22.3 (novel protein similar to a
trypsin
        inhibitor) [Homo sapiens]
        Length = 253

Score = 225 bits (575), Expect = 4e-58
Identities = 109/233 (47%), Positives = 146/233 (63%), Gaps = 8/233 (3%)

Query: 10  RVTTVLFMARAIPAMVVPNATLLEKLLKEYMDEEDGEWWIAKQRGKRAITDNDMQSILDLH 69
        +   | | | | | | | | | | + + | | | | + | | ++| | |
Sbjct: 19  QAVNALIMPNATPAPAQPESTAMRL-----SGLEVPYRKRKRHISVRDMNALLDYH 70

Query: 70  NKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRP 129
        | +|+ | | | | +| | | | | | | | | | +| | | | + | + | | | | | +| |
Sbjct: 71  NHIRASVYPPAANMEYMWVDKRLARAAEAWATQCIWAHGPSQLMRYVGQNLSIHSGQYRS 130

Query: 130 PTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQV VWATSNRIGCAINLCHNM 189
        ++| | +|   + +|   +| | | +| | | | | | | +| | | | +| | | | + | ++
Sbjct: 131 VVDLMKSWSEEKWHYLFAPRDCNPHCPWRCDGPTCSHYTQMVWASSNRLGCAIHTCSSI 190

Query: 190 NIWQGIWPKAVYLVLCNYSKGNWWGHAPYKHGRPCSACPPSFGGGCRENL CYK 242
        ++| | | +| | | | | | + | | | | | + | | | +| | | +| | | | +| +|
Sbjct: 191 SVWGNTWHRAAYLVCNYAIKGNWIGESPYKMGKPCSSCPPSYQGSCNSNMCFK 243
```

The FCTR7 amino acid has 129 of 237 amino acid residues (54%) identical to, and 167 of 237 amino acid residues (70%) similar to, the 258 amino acid 25 kDa Trypsin Inhibitor from *Homo sapiens* (EMBLAcc No.: O43692) (SEQ ID NO:88) (Table 7J).

Table 7J. BLASTP alignments of FCTR7 against 25 kDa Trypsin Inhibitor, (SEQ ID NO:88)

ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - *Homo sapiens* (Human), 258 aa.

Score = 743 (261.5 bits), Expect = 1.6e-73, P = 1.6e-73
Identities = 129/237 (54%), Positives = 167/237 (70%)

The FCTR7 amino acid has 79 of 193 amino acid residues (40%) identical to, and 110 of 193 amino acid residues (56%) similar to, the 266 amino acid Glioma Pathogenesis-Related Protein (RTVP-1 Protein) - *Homo sapiens* (SWISSPROT Acc No.: P48060) (SEQ ID NO:90) (Table 7K).

Table 7K. BLASTP alignments of FCTR7 against Glioma Pathogenesis-Related Protein, (SEQ ID NO:90)

ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1 PROTEIN) - *Homo sapiens* (Human), 266 aa

Score = 314 (110.5 bits), Expect = 4.7e-28, P = 4.7e-28
Identities = 79/193 (40%), Positives = 110/193 (56%)

The FCTR7 amino acid has 66 of 186 amino acid residues (35%) identical to, and 91 of 186 amino acid residues (48%) similar to, the 186 amino acid Neutrophil granules matrix glycoprotein SGP28 precursor from *Homo sapiens* (SWISSPROT Acc No.: S68691) (SEQ ID NO:98) (Table 7L).

Table 7L. BLASTP alignments of FCTR7 against Neutrophil granules matrix glycoprotein, (SEQ ID NO:98)

ptnr:PIR-ID:S68691 neutrophil granules matrix glycoprotein SGP28 precursor - human

Score = 254 (89.4 bits), Expect = 1.1e-21, P = 1.1e-21
Identities = 66/186 (35%), Positives = 91/186 (48%)

A novel developmentally regulated gene with homology to a tumor derived trypsin inhibitor is expressed in lung mesenchyme, as described in Am. J. Physiol. 0:0-0(1999). cDNA cloning of a novel trypsin inhibitor with similarity to pathogenesis-related proteins, and its frequent expression in human brain cancer cells is disclosed in Biochim. Biophys. Acta 1395:202-208(1998). RTVP-1, a novel human gene with sequence similarity to genes of diverse species, is expressed in tumor cell lines of glial but not neuronal origin, as published in Gene 180:125-130(1996). The human glioma pathogenesis-related protein is structurally related to plan pathogenesis-related proteins and its gene is expressed specifically in brain tumors (Gene 159:131-135(1995)). Structure comparison of human glioma pathogenesis-related protein GliPR and the plant pathogenesis-related protein P14a indicates a functional link between the human

immune system and a plant defense system (Proc. Natl. Acad. Sci. U.S.A. 95:2262-2266(1998)). GliPR is highly expressed in the human brain tumor, glioblastoma multiform/astrocytome, but neither in normal fetal or adult brain tissue, nor in other nervous system tumors. GliPR belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1. SGP28, a novel matrix glycoprotein in specific granules of human neutrophils with similarity to a human testis-specific gene product and to a rodent sperm-coating glycoprotein (FEBS Lett. 380, 246-250, 1996). The primary structure and properties of helothermine, a peptide toxin that blocks ryanodine receptors is described in Biophys. J. 68:2280-2288(1995). As GliPR, Helothermine belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1.

Based upon homology, FCTR7 protein and each homologous protein or peptide may share at least some activity.

Therapeutic uses:

FCTR7 protein has homology to trypsin inhibitors, Q91055 helothermine, tumor derived trypsin inhibitors, glioma pathogenesis-related protein, Q9Z0U6 LATE GESTATION LUNG PROTEIN 1, and to the Prosite family which groups mammalian SCP/TPX1; INSECTS AG3/AG5; FUNGI SC7/SC14 AND PLANTS PR-1 proteins. Therefore the FCTR7 protein disclosed in this invention could function like the proteins which it has homology to. These functions include tissue development *in vitro* and *in vivo*, and cancer pathogenesis.

Based the tissue expression pattern, the gene is implicated in diseases of tissues in which it is expressed. These diseases include but are not limited to:

- Glioma,
- cancer,
- lung diseases,
- gestation,
- male and female reproductive diseases,
- deafness,
- neurological disorders,
- gastric disorders, and
- pancreatic diseases like diabetes.

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel FCTR7 substances for use in therapeutic or diagnostic methods.

These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the "Anti-FCTR7 Antibodies" section below. In one embodiment, a contemplated FCTR7 epitope is from aa 40 to 120. In another embodiment, a FCTR7 epitope is from aa 130 to 170. In additional embodiments, FCTR7 epitopes are from aa 210 to 230, and from aa 240 to 280.

TABLE 8A: Summary Of Nucleic Acids And Proteins Of The Invention

Name	Tables	Clone; Description of Homolog	Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO
FCTR1	1A, 1B,	58092213.0.36 follistatin-like protein	1	2
FCTR2	2A, 2B	AC012614_1.0.123; KIAA1061-like protein	3	4
FCTR3	3A, 3B	10129612.0.118; neurestin-like protein	5	6
	3C, 3D	10129612.0.405; neurestin-like protein	7	8
	3E	10129612.0.154; neurestin-like protein	9	
	3F	10129612.0.67; neurestin-like protein	10	
	3G	10129612.0.258; neurestin-like protein	11	
	3H, 3I	10129612.0.352; neurestin-like protein	12	13
FCTR4	4A, 4B	29692275.0.1; NF-Kappa-B P65delta3-like protein	14	15
FCTR5	5A, 5B	32125243.0.21; human complement C1R component precursor -like protein	16	17
	5C, 5D		18	19
FCTR6	6A, 6B	27455183.0.19; novel human blood coagulation factor XI -like protein	20	21
	6C, 6D	27455183.0.145; novel human blood coagulation factor XI -like protein	22	23
FCTR7	7A, 7B	32592466.0.64; trypsin inhibitor -like protein	24	25
FCTR1	Example 2	Ag809 Forward	26	
FCTR1	Example 2	Ag809 Probe	27	
FCTR1	Example 2	Ag809 Reverse	28	
FCTR4	Example 2	Ag2773 Forward	29	
FCTR4	Example 2	Ag2773 Probe	30	
FCTR4	Example 2	Ag2773 Reverse	31	
FCTR5	Example 2	Ag427 Forward	32	
FCTR5	Example 2	Ag427 Probe	33	
FCTR5	Example 2	Ag427 Reverse	34	
FCTR6	Example 2	Ag1541 Forward	35	
FCTR6	Example 2	Ag1541 Probe	36	
FCTR6	Example 2	Ag1541 Reverse	37	

TABLE 8B: Summary of Query Sequences Disclosed

Table	Database	Acc. No.	Sequence Name	Species	SEQ ID NO.
1C, 1K	remtrEmbl	BAA21725	IGFBP-like protein	mouse	38
1D	sptrEmbl	Q61581	Follistatin-like protein-2	Mouse	39

1E	SptrEmbl	Q07822	Mac25 protein	Human	40
1F, 1K	SptrEmbl	U0812	Mac25 protein	Mouse	41
1G, 1K	SptrEmbl	Q16270	Prostacyclin-stimulating factor	Human	42
1H, 1K	PIR	B40098	Colorectal cancer suppressor	Rat	43
1I	TrEmblne w	AAD9360	PTP sigma (brain) precursor	Human	44
1J	SptrEmbl	Q13332	PTP sigma precursor	Human	45
2C	GenBank	AB028984	KIAA1061 cDNA	Human	46
2D	TrEmblne w	BAA85677	KIAA1263	Human	47
2E	TrEmblne w	BAA83013	KIAA1061 protein fragment	Human	48
2F	Embl	CAB70877.1	Hypothetical protein DKFzp566D234.1	Human	49
2G	GenBank	Q62632	Follistatin-related protein-1 precursor	Rat	50
2H	GenBank	Q62536	Follistatin-related protein-1 precursor	Mouse	51
2I	GenBank	JG0187	Follistatin related protein	African clawed frog	52
2J	GenBank	Q12841	Follistatin related protein-1 precursor	Human	53
2K	Embl	CAB42968.1	Flik protein	Chicken	54
2L	GenBank	T13822	Frazzled gene protein	Fruit fly	55
2M	GenBank	AAC38849.1	Roundabout 1	Fruit fly	56
2N	GenBank	O60469	Down Syndrome Cell Adhesion Molecule Precursor	Human	57
2O	SwissProt	Q13449	Limbic system-associated membrane protein precursor	Human	58
2P	SptrEmbl	O70246	Putative neuronal cell adhesion molecule, short form	Mouse	59
2Q	SptrEmbl	O02869	CHLAMP, G11-isoform precursor	Chicken	60
2R	SwissProt	Q62813	Limbic system-associated membrane protein precursor	Rat	61
3J	GenBank	NM_011856.2	Odd Oz/ten-m homology 2	Fruit fly	62
3K	Embl	AJ245711.1	Teneurin-2 cDNA, short splice variant	Chicken	63
3L	GenBank	AB032953	KIAA 1127 cDNA	Human	64
3M, 3U	GenBank	AB025411	Ten-m2 cDNA	Mouse	65
3N	GenBank	NM_020088.1	Neurestin alpha cDNA	Rat	66
3O	Embl	GGA278031	Teneurin-2	Chicken	67
3P	GenBank	NP_035986.2	Odd Oz/ten-m homology 2	Fruit fly	68
3Q	Embl	CAC09416.1	Teneurin-2	Chicken	69
3R	GenBank	BAA77399.1	Ten-m4	Mouse	70
3S	GenBank	AB032953	KIAA1127 protein	Human	71
3T	GenBank	AF086607	Neurestin alpha	Rat	72
4C	SptrEmbl	Q99233	Hypothetical 10 kD protein	Trypanos ome	73
4C	SptrEmbl	Q16896	GABA receptor subunit		74
4C	SptrEmbl	O76473	GABA receptor subunit		75
4C	TrEmblne w	AAD28317	FI3J11.13 protein		76

Text p. 90	SptrEmbl	U13313	NF-kappa B P65 delta 3 prot	Human	77
5E	GenBank	U007061.1	Complement C1R-like proteinase precursor	Human	78
5F	GenBank	NM_001733.1	Complement component 1, R subcomponent cDNA	Human	79
5G	GenBank	AAF44349.1	Complement C1R-like proteinase precursor	Human	80
5H	GenBank	AAA5185.1	Complement C1R component precursor	Human	81
6E	GenBank	AB046651	Brain cDNA clone Qcc-17034	Macaque	82
6F	GenBank	AK09660	Adult testis cDNA, RIKEN full length enriched	Mouse	83
6G	GenBank	AB046651	Hypothetical protein	Macaque	84
6H	GenBank	NP_000838.1	Plasma kallikrein B1 precursor	Human	85
6I	GenBank	BAA37147.1	Kallikrein	Pig	86
6J	Embl	CAA64368.1	Coagulation factor XI	Human	87
7D, 7J	SptrEmbl	O43692	25 kDa trypsin inhibitor	Human	88
7D	SptrEmbl	O44228	HRTT-1		89
7D, 7K	SptrEmbl	P418060	Glioma pathogenesis-related protein	Human	90
7D	PIR-ID	JC4131	Glioma pathogenesis-related protein	Human	91
7D	SwissProt	O19010	Cysteine-rich secretory protein		92
7E	GenBank	AF142573	Putative secretory protein precursor cDNA	Human	93
7F	GenBank	AF142573	Putative secretory protein precursor	Human	94
7G	GenBank	AF109674	Late gestation lung protein 1	Rat	95
7H	GenBank	D45027	R3H domain containing preprotein, 25 kDa trypsin inhibitor	Human	96
7I	Embl	AL117382	Novel protein similar to a trypsin inhibitor	Human	97
7L	PIR-ID	S68691	Neutrophil granules matrix glycoprotein SGP28 precursor	Human	98

FCTR_X Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode FCTR_X polypeptides or biologically-active portions thereof. Also included in the invention are nucleic acid fragments sufficient for use as hybridization probes to identify FCTR_X-encoding nucleic acids (*e.g.*, FCTR_X mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of FCTR_X nucleic acid molecules. As used herein, the term “nucleic acid molecule” is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

An FCTR_X nucleic acid can encode a mature FCTR_X polypeptide. As used herein, a "mature" form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product "mature" form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in which the gene product arises. Examples of such processing steps leading to a "mature" form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a "mature" form of a polypeptide or protein may arise from a step of post-translational modification other than a proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term "probes", as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, *e.g.*, 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term "isolated" nucleic acid molecule, as utilized herein, is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated FCTR_X nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb,

0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell tissue from which the nucleic acid is derived (*e.g.*, brain, heart, liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24 as a hybridization probe, FCTR_X molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to FCTR_X nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion of this nucleotide sequence (*e.g.*, a

fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an FCTR peptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby forming a stable duplex.

As used herein, the term "complementary" refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term "binding" means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95% identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of identical size or

when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those sequences coding for isoforms of FCTR_X polypeptides. Isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for an FCTR_X polypeptide of species other than humans, including, but not limited to: vertebrates, and thus can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat, cow, horse, and other organisms. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the exact nucleotide sequence encoding human FCTR_X protein. Homologous nucleic acid sequences include those nucleic acid sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, as well as a polypeptide possessing FCTR_X biological activity. Various biological activities of the FCTR_X proteins are described below.

An FCTR_X polypeptide is encoded by the open reading frame ("ORF") of an FCTR_X nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set, *e.g.*, a stretch of DNA that would encode a protein of 50 amino acids or more.

The nucleotide sequences determined from the cloning of the human FCTR_X genes allows for the generation of probes and primers designed for use in identifying and/or cloning FCTR_X homologues in other cell types, *e.g.* from other tissues, as well as FCTR_X homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that

hybridizes under stringent conditions to at least about 12, 25, 50, 75, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Probes based on the human FCTR_X nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express an FCTR_X protein, such as by measuring a level of an FCTR_X-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting FCTR_X mRNA levels or determining whether a genomic FCTR_X gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of an FCTR_X polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of FCTR_X" can be prepared by isolating a portion of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that encodes a polypeptide having an FCTR_X biological activity (the biological activities of the FCTR_X proteins are described below), expressing the encoded portion of FCTR_X protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of FCTR_X.

FCTR_X Nucleic Acid and Polypeptide Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, due to degeneracy of the genetic code and thus encode the same FCTR_X proteins as that encoded by the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

In addition to the human FCTR_X nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the FCTR_X

polypeptides may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the FCTR_X genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an FCTR_X protein, preferably a vertebrate FCTR_X protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the FCTR_X genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the FCTR_X polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the FCTR_X polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding FCTR_X proteins from other species, and thus that have a nucleotide sequence that differs from the human sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the FCTR_X cDNAs of the invention can be isolated based on their homology to the human FCTR_X nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (*i.e.*, nucleic acids encoding FCTR_X proteins derived from species other than human) or other related sequences (*e.g.*, paralogs) can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5°C lower than the thermal

melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at T_m, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (*e.g.*, 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. See, *e.g.*, Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (e.g., as employed for cross-species hybridizations). See, e.g., Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* 78: 6789-6792.

Conservative Mutations

In addition to naturally-occurring allelic variants of FCTR_X sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby leading to changes in the amino acid sequences of the encoded FCTR_X proteins, without altering the functional ability of said FCTR_X proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the FCTR_X proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the FCTR_X proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding FCTR_X proteins that contain changes in amino acid residues that are not essential for activity. Such FCTR_X proteins differ in amino acid sequence from SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; more

preferably at least about 70% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; still more preferably at least about 80% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; even more preferably at least about 90% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and most preferably at least about 95% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

An isolated nucleic acid molecule encoding an FCTR_X protein homologous to the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the FCTR_X protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an FCTR_X coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for FCTR_X biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY, FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of

the following: CSA, ATY, SAG, STNK, STPA, SGND, SNDEQ, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

In one embodiment, a mutant FCTR_X protein can be assayed for (i) the ability to form protein:protein interactions with other FCTR_X proteins, other cell-surface proteins, or biologically-active portions thereof, (ii) complex formation between a mutant FCTR_X protein and an FCTR_X ligand; or (iii) the ability of a mutant FCTR_X protein to bind to an intracellular target protein or biologically-active portion thereof; (e.g. avidin proteins).

In yet another embodiment, a mutant FCTR_X protein can be assayed for the ability to regulate a specific biological function (e.g., regulation of insulin release).

10 **Antisense Nucleic Acids**

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire FCTR_X coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an FCTR_X protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; or antisense nucleic acids complementary to an FCTR_X nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an FCTR_X protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the FCTR_X protein. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (i.e., also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding the FCTR_X protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and

Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of FCTR_X mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of FCTR_X mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of FCTR_X mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids (*e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used).

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an FCTR_X protein to thereby inhibit expression of the protein (*e.g.*, by inhibiting transcription and/or translation). The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the

double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (e.g., by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other. See, e.g., Gaultier, *et al.*, 1987. *Nucl. Acids Res.* **15**: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (see, e.g., Inoue, *et al.* 1987. *Nucl. Acids Res.* **15**: 6131-6148) or a chimeric RNA-DNA analogue (see, e.g., Inoue, *et al.*, 1987. *FEBS Lett.* **215**: 327-330).

Ribozymes and PNA Moieties

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* **334**: 585-591) can be used to catalytically cleave FCTR_X mRNA transcripts to thereby inhibit translation of FCTR_X mRNA. A ribozyme having specificity for an FCTR_X-encoding nucleic acid can be designed based upon the nucleotide sequence of an FCTR_X cDNA disclosed herein (i.e., SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an FCTR_X-encoding mRNA. See, e.g., U.S. Patent 4,987,071 to Cech, *et al.* and U.S. Patent

5,116,742 to Cech, *et al.* FCTR_X mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, FCTR_X gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the FCTR_X nucleic acid (*e.g.*, the FCTR_X promoter and/or enhancers) to form triple helical structures that prevent transcription of the FCTR_X gene in target cells. See, *e.g.*, Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the FCTR_X nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. See, *e.g.*, Hyrup, *et al.*, 1996. *Bioorg Med Chem* 4: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (*e.g.*, DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of FCTR_X can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of FCTR_X can also be used, for example, in the analysis of single base pair mutations in a gene (*e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S₁ nucleases (*see*, Hyrup, *et al.*, 1996. *supra*); or as probes or primers for DNA sequence and hybridization (*see*, Hyrup, *et al.*, 1996, *supra*; Perry-O'Keefe, *et al.*, 1996. *supra*).

In another embodiment, PNAs of FCTR_X can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of FCTR_X can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (*e.g.*, RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using

linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (*see*, Hyrup, *et al.*, 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.*, 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA. *See, e.g.*, Mag, *et al.*, 1989. *Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See, e.g.*, Finn, *et al.*, 1996. *supra*. Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. *See, e.g.*, Petersen, *et al.*, 1975. *Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (*see, e.g.*, Letsinger, *et al.*, 1989. *Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al.*, 1987. *Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see, e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see, e.g.*, Krol, *et al.*, 1988. *BioTechniques* 6:958-976) or intercalating agents (*see, e.g.*, Zon, 1988. *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

FCTR_X Polypeptides

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of FCTR_X polypeptides whose sequences are provided in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, while still encoding a protein that maintains its FCTR_X activities and physiological functions, or a functional fragment thereof.

In general, an FCTR_X variant that preserves FCTR_X-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the

invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated FCTR_X proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-FCTR_X antibodies. In one embodiment, native FCTR_X proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, FCTR_X proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, an FCTR_X protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the FCTR_X protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of FCTR_X proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of FCTR_X proteins having less than about 30% (by dry weight) of non-FCTR_X proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-FCTR_X proteins, still more preferably less than about 10% of non-FCTR_X proteins, and most preferably less than about 5% of non-FCTR_X proteins. When the FCTR_X protein or biologically-active portion thereof is recombinantly-produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the FCTR_X protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of FCTR_X proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of FCTR_X proteins having less than about 30% (by dry weight) of chemical precursors or non-FCTR_X chemicals, more preferably less than about 20% chemical precursors or non-FCTR_X chemicals, still more preferably less than about 10% chemical precursors or non-FCTR_X chemicals, and most preferably less than about 5% chemical precursors or non-FCTR_X chemicals.

Biologically-active portions of FCTR proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the FCTR proteins (e.g., the amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25) that include fewer amino acids than the full-length FCTR proteins, and exhibit at least one activity of an FCTR protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the FCTR protein. A biologically-active portion of an FCTR protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native FCTR protein.

In an embodiment, the FCTR protein has an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. In other embodiments, the FCTR protein is substantially homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the FCTR protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the FCTR proteins of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

Determining Homology Between Two or More Sequences

To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position (i.e., as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. See, Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty

of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

5 The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of
10 matched positions by the total number of positions in the region of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

Chimeric and Fusion Proteins

15 The invention also provides FCTR_X chimeric or fusion proteins. As used herein, an FCTR_X "chimeric protein" or "fusion protein" comprises an FCTR_X polypeptide operatively-linked to a non-FCTR_X polypeptide. An "FCTR_X polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an FCTR_X protein (SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25), whereas a "non-FCTR_X polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the
25 FCTR_X protein, *e.g.*, a protein that is different from the FCTR_X protein and that is derived from the same or a different organism. Within an FCTR_X fusion protein the FCTR_X polypeptide can correspond to all or a portion of an FCTR_X protein. In one embodiment, an FCTR_X fusion protein comprises at least one biologically-active portion of an FCTR_X protein. In another embodiment, an FCTR_X fusion protein comprises at least two biologically-active portions of an
30 FCTR_X protein. In yet another embodiment, an FCTR_X fusion protein comprises at least three biologically-active portions of an FCTR_X protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the FCTR_X polypeptide and the non-FCTR_X polypeptide are fused in-frame with one another. The non-FCTR_X polypeptide can be fused to the N-terminus or C-terminus of the FCTR_X polypeptide.

In one embodiment, the fusion protein is a GST-FCTR_X fusion protein in which the FCTR_X sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant FCTR_X polypeptides.

In another embodiment, the fusion protein is an FCTR_X protein containing a heterologous signal sequence at its N-terminus. In certain host cells (e.g., mammalian host cells), expression and/or secretion of FCTR_X can be increased through use of a heterologous signal sequence.

In yet another embodiment, the fusion protein is an FCTR_X-immunoglobulin fusion protein in which the FCTR_X sequences are fused to sequences derived from a member of the immunoglobulin protein family. The FCTR_X-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between an FCTR_X ligand and an FCTR_X protein on the surface of a cell, to thereby suppress FCTR_X-mediated signal transduction *in vivo*. The FCTR_X-immunoglobulin fusion proteins can be used to affect the bioavailability of an FCTR_X cognate ligand. Inhibition of the FCTR_X ligand/FCTR_X interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, as well as modulating (e.g. promoting or inhibiting) cell survival. Moreover, the FCTR_X-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-FCTR_X antibodies in a subject, to purify FCTR_X ligands, and in screening assays to identify molecules that inhibit the interaction of FCTR_X with an FCTR_X ligand.

An FCTR_X chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, e.g., by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., Ausubel, *et al.* (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An FCTR_X-encoding nucleic acid

can be cloned into such an expression vector such that the fusion polypeptide is linked in-frame to the FCTR_X protein.

FCTR_X Agonists and Antagonists

The invention also pertains to variants of the FCTR_X proteins that function as either FCTR_X agonists (*i.e.*, mimetics) or as FCTR_X antagonists. Variants of the FCTR_X protein can be generated by mutagenesis (*e.g.*, discrete point mutation or truncation of the FCTR_X protein). An agonist of the FCTR_X protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the FCTR_X protein. An antagonist of the FCTR_X protein can inhibit one or more of the activities of the naturally occurring form of the FCTR_X protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the FCTR_X protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the FCTR_X proteins.

Variants of the FCTR_X proteins that function as either FCTR_X agonists (*i.e.*, mimetics) or as FCTR_X antagonists can be identified by screening combinatorial libraries of mutants (*e.g.*, truncation mutants) of the FCTR_X proteins for FCTR_X protein agonist or antagonist activity. In one embodiment, a variegated library of FCTR_X variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of FCTR_X variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential FCTR_X sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of FCTR_X sequences therein. There are a variety of methods which can be used to produce libraries of potential FCTR_X variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential FCTR_X sequences. Methods for synthesizing degenerate oligonucleotides are well-known within the art. *See, e.g.*, Narang, 1983. *Tetrahedron* 39: 3; Itakura, *et al.*, 1984. *Annu. Rev. Biochem.* 53: 323; Itakura, *et al.*, 1984. *Science* 198: 1056; Ike, *et al.*, 1983. *Nucl. Acids Res.* 11: 477.

In addition, libraries of fragments of the FCTR_X protein coding sequences can be used to generate a variegated population of FCTR_X fragments for screening and subsequent selection of variants of an FCTR_X protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an FCTR_X coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S₁ nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can be derived which encodes N-terminal and internal fragments of various sizes of the FCTR_X proteins.

Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of FCTR_X proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify FCTR_X variants. *See, e.g.,* Arkin and Yourvan, 1992. *Proc. Natl. Acad. Sci. USA* 89: 7811-7815; Delgrave, *et al.*, 1993. *Protein Engineering* 6:327-331.

Anti-FCTR_X Antibodies

The invention encompasses antibodies and antibody fragments, such as F_{ab} or (F_{ab})₂, that bind immunospecifically to any of the FCTR_X polypeptides of said invention.

An isolated FCTR_X protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind to FCTR_X polypeptides using standard techniques for polyclonal and monoclonal antibody preparation. The full-length FCTR_X proteins can be used or, alternatively, the invention provides antigenic peptide fragments of FCTR_X proteins for use as immunogens. The antigenic FCTR_X peptides comprises at least 4 amino acid residues of the amino acid sequence shown in SEQ ID NO NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and

encompasses an epitope of FCTR_X such that an antibody raised against the peptide forms a specific immune complex with FCTR_X. Preferably, the antigenic peptide comprises at least 6, 8, 10, 15, 20, or 30 amino acid residues. Longer antigenic peptides are sometimes preferable over shorter antigenic peptides, depending on use and according to methods well known to someone skilled in the art.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of FCTR_X that is located on the surface of the protein (*e.g.*, a hydrophilic region). As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation (*see, e.g.*, Hopp and Woods, 1981. *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle, 1982. *J. Mol. Biol.* 157: 105-142, each incorporated herein by reference in their entirety).

As disclosed herein, FCTR_X protein sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or derivatives, fragments, analogs or homologs thereof, may be utilized as immunogens in the generation of antibodies that immunospecifically-bind these protein components. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically-active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically-binds (immunoreacts with) an antigen, such as FCTR_X. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab} and F_{(ab')₂} fragments, and an F_{ab} expression library. In a specific embodiment, antibodies to human FCTR_X proteins are disclosed. Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies to an FCTR_X protein sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a derivative, fragment, analog or homolog thereof. Some of these proteins are discussed below.

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by injection with the native protein, or a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed FCTR_X protein or a chemically-synthesized FCTR_X polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as *Bacille Calmette-Guerin* and *Corynebacterium parvum*, or similar

immunostimulatory agents. If desired, the antibody molecules directed against FCTR_X can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of FCTR_X. A monoclonal antibody composition thus typically displays a single binding affinity for a particular FCTR_X protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular FCTR_X protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (*see, e.g.*, Kohler & Milstein, 1975. *Nature* 256: 495-497); the trioma technique; the human B-cell hybridoma technique (*see, e.g.*, Kozbor, *et al.*, 1983. *Immunol. Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (*see, e.g.*, Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the invention and may be produced by using human hybridomas (*see, e.g.*, Cote, *et al.*, 1983. *Proc Natl Acad Sci USA* 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus *in vitro* (*see, e.g.*, Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Each of the above citations is incorporated herein by reference in their entirety.

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an FCTR_X protein (*see, e.g.*, U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (*see, e.g.*, Huse, *et al.*, 1989. *Science* 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for an FCTR_X protein or derivatives, fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. *See, e.g.*, U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotypes to an FCTR_X protein may be produced by techniques known in the art including, but not limited to: (i) an F_(ab)₂ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an F_(ab)₂ fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent; and (iv) F_v fragments.

Additionally, recombinant anti-FCTR_X antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made

using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; U.S. Pat. No. 5,225,539; European Patent Application No. 125,023; Better, *et al.*, 1988. *Science* 240: 1041-1043; Liu, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 3439-3443; Liu, *et al.*, 1987. *J. Immunol.* 139: 3521-3526; Sun, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 214-218; Nishimura, *et al.*, 1987. *Cancer Res.* 47: 999-1005; Wood, *et al.*, 1985. *Nature* 314 :446-449; Shaw, *et al.*, 1988. *J. Natl. Cancer Inst.* 80: 1553-1559); Morrison(1985) *Science* 229:1202-1207; Oi, *et al.* (1986) *BioTechniques* 4:214; Jones, *et al.*, 1986. *Nature* 321: 552-525; Verhoeyan, *et al.*, 1988. *Science* 239: 1534; and Beidler, *et al.*, 1988. *J. Immunol.* 141: 4053-4060. Each of the above citations are incorporated herein by reference in their entirety.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an FCTR_X protein is facilitated by generation of hybridomas that bind to the fragment of an FCTR_X protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an FCTR_X protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-FCTR_X antibodies may be used in methods known within the art relating to the localization and/or quantitation of an FCTR_X protein (*e.g.*, for use in measuring levels of the FCTR_X protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for FCTR_X proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

An anti-FCTR_X antibody (*e.g.*, monoclonal antibody) can be used to isolate an FCTR_X polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-FCTR_X antibody can facilitate the purification of natural FCTR_X polypeptide from cells and of recombinantly-produced FCTR_X polypeptide expressed in host cells. Moreover, an anti-FCTR_X antibody can be used to detect FCTR_X protein (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the FCTR_X protein. Anti-FCTR_X antibodies can be used diagnostically to monitor protein levels in tissue as part of a

clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

FCTR_X Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an FCTR_X protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis

of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably-linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, FCTR_X proteins, mutant forms of FCTR_X proteins, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of FCTR_X proteins in prokaryotic or eukaryotic cells. For example, FCTR_X proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: (i) to increase expression of recombinant protein; (ii) to increase the solubility of the recombinant protein; and (iii) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa,

thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

5 Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 60-89).

10 One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein. See, e.g., Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (see, e.g., Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

15 In another embodiment, the FCTR_X expression vector is a yeast expression vector. Examples of vectors for expression in yeast *Saccharomyces cerevisiae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30: 933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (InVitrogen Corp, San Diego, Calif.).

20 Alternatively, FCTR_X can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

25 In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, e.g., Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477), pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, e.g., the murine hox promoters (Kessel and Gruss, 1990. *Science* 249: 374-379) and the α -fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to FCTRX mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see, e.g., Weintraub, *et al.*, "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental

influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, FCTR_X protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.*, resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding FCTR_X or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) FCTR_X protein. Accordingly, the invention further provides methods for producing FCTR_X protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding FCTR_X protein has been introduced) in a suitable medium such that FCTR_X protein is produced. In another embodiment, the method further comprises isolating FCTR_X protein from the medium or the host cell.

Transgenic FCTR_X Animals

The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which FCTR_X protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous FCTR_X sequences have been introduced into their genome or homologous recombinant animals in which endogenous FCTR_X sequences have been altered. Such animals are useful for studying the function and/or activity of FCTR_X protein and for identifying and/or evaluating modulators of FCTR_X protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome of a cell from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous FCTR_X gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing FCTR_X-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human FCTR_X cDNA sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be introduced as a transgene into the genome of a non-human animal. Alternatively, a non-human homologue of the human FCTR_X gene, such as a mouse FCTR_X gene, can be isolated based on hybridization to the human FCTR_X cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the FCTR_X transgene to direct expression of FCTR_X protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A

transgenic founder animal can be identified based upon the presence of the FCTR_X transgene in its genome and/or expression of FCTR_X mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding FCTR_X protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an FCTR_X gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the FCTR_X gene. The FCTR_X gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24), but more preferably, is a non-human homologue of a human FCTR_X gene. For example, a mouse homologue of human FCTR_X gene of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be used to construct a homologous recombination vector suitable for altering an endogenous FCTR_X gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous FCTR_X gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous FCTR_X gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous FCTR_X protein). In the homologous recombination vector, the altered portion of the FCTR_X gene is flanked at its 5'- and 3'-termini by additional nucleic acid of the FCTR_X gene to allow for homologous recombination to occur between the exogenous FCTR_X gene carried by the vector and an endogenous FCTR_X gene in an embryonic stem cell. The additional flanking FCTR_X nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5'- and 3'-termini) are included in the vector. *See, e.g.*, Thomas, *et al.*, 1987. *Cell* 51: 503 for a description of homologous recombination vectors. The vector is then introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced FCTR_X gene has homologously-recombined with the endogenous FCTR_X gene are selected. *See, e.g.*, Li, *et al.*, 1992. *Cell* 69: 915.

The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras. *See, e.g.*, Bradley, 1987. In: TERATOCARCINOMAS AND EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp. 113-152. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously-recombined DNA in their germ cells can

be used to breed animals in which all cells of the animal contain homologously-recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol.* 2: 823-829; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, See, e.g., Lakso, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae*. See, O'Gorman, *et al.*, 1991. *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al.*, 1997. *Nature* 385: 810-813. In brief, a cell (e.g., a somatic cell) from the transgenic animal can be isolated and induced to exit the growth cycle and enter G₀ phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell (e.g., the somatic cell) is isolated.

Pharmaceutical Compositions

The FCTR_X nucleic acid molecules, FCTR_X proteins, and anti-FCTR_X antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like,

compatible with pharmaceutical administration. Suitable carriers are described in the most recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (*i.e.*, topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the

action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, an FCTR_X protein or anti-FCTR_X antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for

example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

5 The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

10 In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes
15 targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

20 It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and
25 the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

30 The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.*, U.S. Patent No. 5,328,470) or by stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant

cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

5 **Screening and Detection Methods**

10 The isolated nucleic acid molecules of the invention can be used to express FCTR_X protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect FCTR_X mRNA (*e.g.*, in a biological sample) or a genetic lesion in an FCTR_X gene, and to modulate FCTR_X activity, as described further, below. In addition, the FCTR_X proteins can be used to screen drugs or compounds that modulate the FCTR_X protein activity or expression as well as to treat disorders characterized by insufficient or excessive production of FCTR_X protein or production of FCTR_X protein forms that have decreased or aberrant activity compared to FCTR_X wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the metabolic syndrome X as well as anorexia and wasting disorders associated with chronic diseases and various cancers, and infectious disease (possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-FCTR_X antibodies of the invention can be used to detect and isolate FCTR_X proteins and modulate FCTR_X activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

15 The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

Screening Assays

20 The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to FCTR_X proteins or have a stimulatory or inhibitory effect on, *e.g.*, FCTR_X protein expression or FCTR_X protein activity. The invention also includes compounds identified in the screening assays described herein.

25 In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of an FCTR_X protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid

phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. See, e.g., Lam, 1997. *Anticancer Drug Design* 12: 145.

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be, e.g., nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2059; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.

Libraries of compounds may be presented in solution (e.g., Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an FCTR_X protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the FCTR_X protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the FCTR_X protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with ¹²⁵I, ³⁵S, ¹⁴C, or ³H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can

be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds FCTR_X to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the test compound to preferentially bind to FCTR_X protein or a biologically-active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the FCTR_X protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTR_X or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule. As used herein, a "target molecule" is a molecule with which an FCTR_X protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses an FCTR_X interacting protein, a molecule on the surface of a second cell, a molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. An FCTR_X target molecule can be a non-FCTR_X molecule or an FCTR_X protein or polypeptide of the invention. In one embodiment, an FCTR_X target molecule is a component of a signal transduction pathway that facilitates transduction of an extracellular signal (*e.g.* a signal generated by binding of a compound to a membrane-bound FCTR_X molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with FCTR_X.

Determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.* intracellular Ca²⁺, diacylglycerol, IP₃, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the

induction of a reporter gene (comprising an FCTR_X-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting an FCTR_X protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the FCTR_X protein or biologically-active portion thereof. Binding of the test compound to the FCTR_X protein can be determined either directly or indirectly as described above. In one such embodiment, the assay comprises contacting the FCTR_X protein or biologically-active portion thereof with a known compound which binds FCTR_X to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the test compound to preferentially bind to FCTR_X or biologically-active portion thereof as compared to the known compound.

In still another embodiment, an assay is a cell-free assay comprising contacting FCTR_X protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (*e.g.* stimulate or inhibit) the activity of the FCTR_X protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTR_X can be accomplished, for example, by determining the ability of the FCTR_X protein to bind to an FCTR_X target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of FCTR_X protein can be accomplished by determining the ability of the FCTR_X protein further modulate an FCTR_X target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra*.

In yet another embodiment, the cell-free assay comprises contacting the FCTR_X protein or biologically-active portion thereof with a known compound which binds FCTR_X protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the FCTR_X protein to preferentially bind to or modulate the activity of an FCTR_X target molecule.

The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of FCTR_X protein. In the case of cell-free assays comprising the membrane-bound form of FCTR_X protein, it may be desirable to utilize a solubilizing agent such

that the membrane-bound form of FCTR_X protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton[®] X-100, Triton[®] X-114, Thesit[®], Isotridecypoly(ethylene glycol ether)_n, N-dodecyl--
5 N,N-dimethyl-3-ammonio-1-propane sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either FCTR_X protein or its target molecule to facilitate separation of
10 complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to FCTR_X protein, or interaction of FCTR_X protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a
15 fusion protein can be provided that adds a domain that allows one or both of the proteins to be bound to a matrix. For example, GST-FCTR_X fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or FCTR_X protein, and the mixture is
20 incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex determined either directly or indirectly, for example, as described, *supra*. Alternatively, the complexes can be dissociated from the matrix, and the level of FCTR_X protein binding or activity determined
25 using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the FCTR_X protein or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated FCTR_X protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques
30 well-known within the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with FCTR_X protein or target molecules, but which do not interfere with binding of the FCTR_X protein to its target molecule, can be derivatized to the wells of the plate, and unbound target or FCTR_X protein trapped in the wells by antibody conjugation. Methods

for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the FCTR_X protein or target molecule, as well as enzyme-linked assays that rely on detecting an enzymatic activity associated with the FCTR_X protein or target molecule.

5 In another embodiment, modulators of FCTR_X protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of FCTR_X mRNA or protein in the cell is determined. The level of expression of FCTR_X mRNA or protein in the presence of the candidate compound is compared to the level of expression of FCTR_X mRNA or protein in the absence of the candidate compound. The candidate compound can then
10 be identified as a modulator of FCTR_X mRNA or protein expression based upon this comparison. For example, when expression of FCTR_X mRNA or protein is greater (*i.e.*, statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of FCTR_X mRNA or protein expression. Alternatively, when expression of FCTR_X mRNA or protein is less (statistically significantly
15 less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of FCTR_X mRNA or protein expression. The level of FCTR_X mRNA or protein expression in the cells can be determined by methods described herein for detecting FCTR_X mRNA or protein.

In yet another aspect of the invention, the FCTR_X proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos, *et al.*, 1993. *Cell* 72: 223-232; Madura, *et al.*, 1993. *J. Biol. Chem.* 268: 12046-12054; Bartel, *et al.*, 1993. *Biotechniques* 14: 920-924; Iwabuchi, *et al.*, 1993. *Oncogene* 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with FCTR_X ("FCTR_X-binding
20 proteins" or "FCTR_X-bp") and modulate FCTR_X activity. Such FCTR_X-binding proteins are also likely to be involved in the propagation of signals by the FCTR_X proteins as, for example, upstream or downstream elements of the FCTR_X pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for FCTR_X is fused to a gene
30 encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an FCTR_X-dependent complex, the DNA-binding and activation domains of the transcription factor

are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with FCTR_X.

The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

Detection Assays

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. By way of example, and not of limitation, these sequences can be used to: (i) map their respective genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the FCTR_X sequences, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments or derivatives thereof, can be used to map the location of the FCTR_X genes, respectively, on a chromosome. The mapping of the FCTR_X sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, FCTR_X genes can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the FCTR_X sequences. Computer analysis of the FCTR_X sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the FCTR_X sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (*e.g.*, human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in which human

cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. See, e.g., D'Eustachio, *et al.*, 1983. *Science* 220: 919-924. Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the FCTR_X sequences to design oligonucleotide primers, sub-localization can be achieved with panels of fragments from specific chromosomes.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases, will suffice to get good results at a reasonable amount of time. For a review of this technique, see, Verma, *et al.*, HUMAN CHROMOSOMES: A MANUAL OF BASIC TECHNIQUES (Pergamon Press, New York 1988).

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, e.g., in McKusick, MENDELIAN INHERITANCE IN MAN, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis

(co-inheritance of physically adjacent genes), described in, *e.g.*, *Thelander, et al.*, 1987. *Nature*, 325: 783-787.

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the FCTR_X gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

Tissue Typing

The FCTR_X sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the FCTR_X sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The FCTR_X sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to

differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining FCTR_X protein and/or nucleic acid expression as well as FCTR_X activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant FCTR_X expression or activity. The disorders include Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The invention also provides for prognostic

(or predictive) assays for determining whether an individual is at risk of developing a disorder associated with FCTR_X protein, nucleic acid expression or activity. For example, mutations in an FCTR_X gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with FCTR_X protein, nucleic acid expression, or biological activity.

Another aspect of the invention provides methods for determining FCTR_X protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics").

Pharmacogenomics allows for the selection of agents (*e.g.*, drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (*e.g.*, the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTR_X in clinical trials.

These and other agents are described in further detail in the following sections.

Diagnostic Assays

An exemplary method for detecting the presence or absence of FCTR_X in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting FCTR_X protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes FCTR_X protein such that the presence of FCTR_X is detected in the biological sample. An agent for detecting FCTR_X mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to FCTR_X mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length FCTR_X nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to FCTR_X mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting FCTR_X protein is an antibody capable of binding to FCTR_X protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (*e.g.*, Fab or F(ab')₂) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a

primary antibody using fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect FCTR_X mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of FCTR_X mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of FCTR_X protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of FCTR_X genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of FCTR_X protein include introducing into a subject a labeled anti-FCTR_X antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting FCTR_X protein, mRNA, or genomic DNA, such that the presence of FCTR_X protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of FCTR_X protein, mRNA or genomic DNA in the control sample with the presence of FCTR_X protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of FCTR_X in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting FCTR_X protein or mRNA in a biological sample; means for determining the amount of FCTR_X in the sample; and means for comparing the amount of FCTR_X in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect FCTR_X protein or nucleic acid.

Prognostic Assays

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant FCTR_X expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a

disorder associated with FCTR^X protein, nucleic acid expression activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a method for identifying a disease or disorder associated with aberrant FCTR^X expression or activity in which a test sample is obtained from a subject and FCTR^X protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of FCTR^X protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant FCTR^X expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant FCTR^X expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant FCTR^X expression or activity in which a test sample is obtained and FCTR^X protein or nucleic acid is detected (*e.g.*, wherein the presence of FCTR^X protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant FCTR^X expression or activity).

The methods of the invention can also be used to detect genetic lesions in an FCTR^X gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant cell proliferation and/or differentiation. In various embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding an FCTR^X-protein, or the misexpression of the FCTR^X gene. For example, such genetic lesions can be detected by ascertaining the existence of at least one of: (i) a deletion of one or more nucleotides from an FCTR^X gene; (ii) an addition of one or more nucleotides to an FCTR^X gene; (iii) a substitution of one or more nucleotides of an FCTR^X gene, (iv) a chromosomal rearrangement of an FCTR^X gene; (v) an alteration in the level of a messenger RNA transcript of an FCTR^X gene, (vi) aberrant modification of an FCTR^X gene, such as of the methylation pattern of the genomic DNA, (vii) the presence of a non-wild-type splicing pattern of a messenger RNA transcript of an FCTR^X gene, (viii) a non-wild-type level of an FCTR^X protein, (ix) allelic loss of an FCTR^X gene, and (x) inappropriate post-translational modification of an FCTR^X protein. As described herein, there are a large number of assay techniques known

in the art which can be used for detecting lesions in an FCTR gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

5 In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point
10 mutations in the FCTR gene (*see*, Abravaya, *et al.*, 1995. *Nucl. Acids Res.* 23: 675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers that specifically hybridize to an FCTR gene under conditions such that hybridization and amplification of the FCTR gene (if present) occurs, and detecting the
15 presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see*,
20 Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional amplification system (*see*, Kwoh, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Q β Replicase (*see*, Lizardi, *et al.*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid
25 molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in an FCTR gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared.
30 Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.*, U.S. Patent No. 5,493,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in FCTR_X can be identified by hybridizing a sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing hundreds or thousands of oligonucleotide probes. *See, e.g.*, Cronin, *et al.*, 1996. *Human Mutation* 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic mutations in FCTR_X can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, *et al.*, *supra*. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the FCTR_X gene and detect mutations by comparing the sequence of the sample FCTR_X with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci. USA* 74: 5463. It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (*see, e.g.*, Naeve, *et al.*, 1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (*see, e.g.*, PCT International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36: 127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the FCTR_X gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes. *See, e.g.*, Myers, *et al.*, 1985. *Science* 230: 1242. In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by hybridizing (labeled) RNA or DNA containing the wild-type FCTR_X sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with S₁ nuclease to enzymatically digest the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then

separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton, *et al.*, 1988. *Proc. Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.*, 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

5 In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in FCTR_X cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at
10 G/T mismatches. See, e.g., Hsu, *et al.*, 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on an FCTR_X sequence, e.g., a wild-type FCTR_X sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

15 In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in FCTR_X genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids. See, e.g., Orita, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79. Single-stranded
20 DNA fragments of sample and control FCTR_X nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is
25 more sensitive to a change in sequence. In one embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. See, e.g., Keen, *et al.*, 1991. *Trends Genet.* 7: 5.

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel
30 electrophoresis (DGGE). See, e.g., Myers, *et al.*, 1985. *Nature* 313: 495. When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient

to identify differences in the mobility of control and sample DNA. See, e.g., Rosenbaum and Reissner, 1987. *Biophys. Chem.* 265: 12753.

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension.

5 For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit hybridization only if a perfect match is found. See, e.g., Saiki, *et al.*, 1986. *Nature* 324: 163; Saiki, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 6230. Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached
10 to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; see, e.g., Gibbs, *et al.*, 1989. *Nucl. Acids Res.* 17: 2437-2448) or at the extreme 3'-terminus of one primer where, under appropriate
15 conditions, mismatch can prevent, or reduce polymerase extension (see, e.g., Prossner, 1993. *Tibtech.* 11: 238). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. See, e.g., Gasparini, *et al.*, 1992. *Mol. Cell Probes* 6: 1. It is anticipated that in certain embodiments amplification may also be
20 performed using *Taq* ligase for amplification. See, e.g., Barany, 1991. *Proc. Natl. Acad. Sci. USA* 88: 189. In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged
25 diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving an FCTR_X gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which FCTR_X is expressed may be utilized in the prognostic assays described herein. However, any
30 biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

Pharmacogenomics

Agents, or modulators that have a stimulatory or inhibitory effect on FCTR_X activity (e.g., FCTR_X gene expression), as identified by a screening assay described herein can be

administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g., Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy) In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered.

Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of FCTR_X protein, expression of FCTR_X nucleic acid, or mutation content of FCTR_X genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See *e.g.*,

Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-988. Zanger, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of FCTR_X protein, expression of FCTR_X nucleic acid, or mutation content of FCTR_X genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with an FCTR_X modulator, such as a modulator identified by one of the exemplary screening assays described herein.

Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTR_X (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase FCTR_X gene expression, protein levels, or upregulate FCTR_X activity, can be monitored in clinical trials of subjects exhibiting decreased FCTR_X gene expression, protein levels, or downregulated FCTR_X activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease FCTR_X gene expression, protein levels, or downregulate FCTR_X activity, can be monitored in clinical trials of subjects exhibiting increased FCTR_X gene expression, protein levels, or upregulated FCTR_X activity. In such clinical trials, the expression or activity of FCTR_X and, preferably, other genes that have been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

By way of example, and not of limitation, genes, including FCTR_X, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates FCTR_X activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of FCTR_X and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of FCTR_X or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of an FCTR_X protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the FCTR_X protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing

the level of expression or activity of the FCTR~~X~~ protein, mRNA or genomic DNA in the pre-administration sample with the FCTR~~X~~ protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of FCTR~~X~~ to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of FCTR~~X~~ to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant FCTR~~X~~ expression or activity. The disorders include cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation, idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright Hereditary Osteodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

Disease and Disorders

Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (i) an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; (ii) antibodies to an aforementioned peptide; (iii) nucleic acids encoding an aforementioned peptide; (iv) administration of antisense nucleic acid and nucleic acids that are "dysfunctional" (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to "knockout" endogenous function of an aforementioned peptide by homologous recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (v) modulators (*i.e.*, inhibitors, agonists and antagonists, including

additional peptide mimetic of the invention or antibodies specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with
5 Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

Increased or decreased levels can be readily detected by quantifying peptide and/or RNA,
10 by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for RNA or peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or
15 hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot blots, *in situ* hybridization, and the like).

Prophylactic Methods

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant FCTR_X expression or activity, by administering to the
20 subject an agent that modulates FCTR_X expression or at least one FCTR_X activity. Subjects at risk for a disease that is caused or contributed to by aberrant FCTR_X expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the FCTR_X aberrancy, such that a disease or disorder is prevented or,
25 alternatively, delayed in its progression. Depending upon the type of FCTR_X aberrancy, for example, an FCTR_X agonist or FCTR_X antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

Therapeutic Methods

30 Another aspect of the invention pertains to methods of modulating FCTR_X expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of FCTR_X protein activity associated with the cell. An agent that modulates FCTR_X protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of an

FCTR_X protein, a peptide, an FCTR_X peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more FCTR_X protein activity. Examples of such stimulatory agents include active FCTR_X protein and a nucleic acid molecule encoding FCTR_X that has been introduced into the cell. In another embodiment, the agent inhibits one or more FCTR_X protein activity. Examples of such inhibitory agents include antisense FCTR_X nucleic acid molecules and anti-FCTR_X antibodies. These modulatory methods can be performed *in vitro* (e.g., by culturing the cell with the agent) or, alternatively, *in vivo* (e.g., by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of an FCTR_X protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., up-regulates or down-regulates) FCTR_X expression or activity. In another embodiment, the method involves administering an FCTR_X protein or nucleic acid molecule as therapy to compensate for reduced or aberrant FCTR_X expression or activity.

Stimulation of FCTR_X activity is desirable in situations in which FCTR_X is abnormally downregulated and/or in which increased FCTR_X activity is likely to have a beneficial effect. One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (e.g., cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (e.g., preclampsia).

Determination of the Biological Effect of the Therapeutic

In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo* testing, any of the animal model system known in the art may be used prior to administration to human subjects.

Prophylactic and Therapeutic Uses of the Compositions of the Invention

The FCTR_X nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not limited to: Also within the scope of the invention is the use of a Therapeutic in the manufacture

of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, Turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bücklers corneal dystrophy.

As an example, a cDNA encoding the FCTR protein of the invention may be useful in gene therapy, and the protein may be useful when administered to a subject in need thereof. By way of non-limiting example, the compositions of the invention will have efficacy for treatment of patients suffering from: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways

resulting in tumor escape from immune surveillance, neurologic disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

Both the novel nucleic acid encoding the FCTR_X protein, and the FCTR_X protein of the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.*, some peptides have been found to possess anti-bacterial properties). These materials are further useful in the generation of antibodies which immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

EXAMPLES

The following examples illustrate by way of non-limiting example various aspects of the invention.

The following examples illustrate by way of non-limiting example various aspects of the invention.

Example 1: Method of Identifying the Nucleic Acids

The novel nucleic acids of the invention were identified by TblastN using a proprietary sequence file, run against the Genomic Daily Files made available by GenBank. The nucleic acids were further predicted by the proprietary software program GenScan™, including selection of exons. These were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length proteins.

Example 2. Quantitative expression analysis of FCTR2 in various cells and tissues

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR; TAQMAN®). RTQ PCR was performed on a Perkin-Elmer Biosystems ABI PRISM® 7700 Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing cells and cell lines from normal and cancer sources), Panel 2 (containing samples derived from tissues, in particular from surgical samples, from normal and cancer sources), Panel 3 (containing samples derived from a wide variety of cancer sources) and Panel 4 (containing cells and cell lines from normal cells and cells related to inflammatory conditions).

First, the RNA samples were normalized to constitutively expressed genes such as β -actin and GAPDH. RNA (~50 ng total or ~1 ng polyA+) was converted to cDNA using the TAQMAN® Reverse Transcription Reagents Kit (PE Biosystems, Foster City, CA; Catalog No. N808-0234) and random hexamers according to the manufacturer's protocol. Reactions were performed in 20 μ l and incubated for 30 min. at 48°C. cDNA (5 μ l) was then transferred to a separate plate for the TAQMAN® reaction using β -actin and GAPDH TAQMAN® Assay Reagents (PE Biosystems; Catalog Nos. 4310881E and 4310884E, respectively) and TAQMAN® universal PCR Master Mix (PE Biosystems; Catalog No. 4304447) according to the manufacturer's protocol. Reactions were performed in 25 μ l using the following parameters: 2 min. at 50°C; 10 min. at 95°C; 15 sec. at 95°C/1 min. at 60°C (40 cycles). Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100. The average CT values obtained for β -actin and GAPDH were used to normalize RNA samples. The RNA sample generating the highest CT value required no further diluting, while all other samples were diluted relative to this sample according to their β -actin /GAPDH average CT values.

Normalized RNA (5 μ l) was converted to cDNA and analyzed via TAQMAN® using One Step RT-PCR Master Mix Reagents (PE Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions. Probes and primers were designed for each assay according to Perkin Elmer Biosystem's *Primer Express* Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following

parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (T_m) range = 58°-60° C, primer optimal T_m = 59° C, maximum primer difference = 2° C, probe does not have 5' G, probe T_m must be 10° C greater than primer T_m , amplicon size 75 bp to 100 bp. The probes and primers selected (see below) were synthesized by Synthesgen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900 nM each, and probe, 200nM.

PCR conditions: Normalized RNA from each tissue and each cell line was spotted in each well of a 96 well PCR plate (Perkin Elmer Biosystems). PCR cocktails including two probes (a probe specific for the target clone and another gene-specific probe multiplexed with the target probe) were set up using 1X TaqMan™ PCR Master Mix for the PE Biosystems 7700, with 5 mM MgCl₂, dNTPs (dA, G, C, U at 1:1:1:2 ratios), 0.25 U/ml AmpliTaq Gold™ (PE Biosystems), and 0.4 U/μl RNase inhibitor, and 0.25 U/μl reverse transcriptase. Reverse transcription was performed at 48° C for 30 minutes followed by amplification/PCR cycles as follows: 95° C 10 min, then 40 cycles of 95° C for 15 seconds, 60° C for 1 minute.

In the results for Panel 1, the following abbreviations are used:

ca. = carcinoma,
* = established from metastasis,
met = metastasis,
s cell var= small cell variant,
non-s = non-sm =non-small,
squamous = squamous,
pl. eff = pl effusion = pleural effusion,
glio = glioma,
astro = astrocytoma, and
neuro = neuroblastoma.

Panel 2

The plates for Panel 2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation

with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologists at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissue were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

Panel 4

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4r) or cDNA (Panel 4d) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues such as colon and lung (Stratagene ,La Jolla, CA) and thymus and kidney (Clontech) were employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and grown in the media supplied for these cell types by Clonetics. These primary cell types were activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as indicated. The following cytokines were used; IL-1 beta at approximately 1-5 ng/ml, TNF alpha at approximately 5-10 ng/ml, IFN gamma at approximately 20-50 ng/ml, IL-4 at approximately 5-10 ng/ml, IL-9 at approximately 5-10 ng/ml, IL-13 at approximately 5-10 ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal media from Clonetics with 0.1% serum.

Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20 ng/ml PMA and 1-2 μ g/ml ionomycin, IL-12 at 5-10 ng/ml, IFN gamma at 20-50 ng/ml and IL-18 at 5-10 ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) with PHA (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5 μ g/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately 2×10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol (5.5×10^{-5} M) (Gibco), and 10 mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions. Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum (FCS) (Hyclone, Logan, UT), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate

(Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM HEPES (Gibco), 50 ng/ml GM-CSF and 5 ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM HEPES (Gibco) and 10% AB Human Serum or MCSF at approximately 50 ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at 100 ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10 μ g/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and +ve selection. Then CD45RO beads were used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM HEPES (Gibco) and plated at 10^6 cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5 μ g/ml anti-CD28 (Pharmingen) and 3 μ g/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, we activated the isolated CD8 lymphocytes for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM HEPES (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM HEPES (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resuspended at 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids

(Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco). To activate the cells, we used PWM at 5 µg/ml or anti-CD40 (Pharmingen) at approximately 10 µg/ml and IL-4 at 5-10 ng/ml. Cells were harvested for RNA preparation at 24, 48 and 72 hours.

To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10 µg/ml anti-CD28 (Pharmingen) and 2 µg/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at 10^5 - 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (4 ng/ml). IL-12 (5 ng/ml) and anti-IL4 (1 µg/ml) were used to direct to Th1, while IL-4 (5 ng/ml) and anti-IFN gamma (1 µg/ml) were used to direct to Th2 and IL-10 at 5 ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (1 ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1 µg/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1 mM dbcAMP at 5×10^5 cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to 5×10^5 cells/ml. For the culture of these cells, we used DMEM or RPMI (as recommended by the ATCC), with the addition of 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10 ng/ml and ionomycin at 1 µg/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-

H292 were also obtained from the ATCC. Both were cultured in MEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5 x 10⁻⁵ M (Gibco), and 10 mM Hepes (Gibco). CCD1106 cells were activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and 1 ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5 ng/ml IL-4, 5 ng/ml IL-9, 5 ng/ml IL-13 and 25 ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately 10⁷ cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15 ml Falcon Tube. An equal volume of isopropanol was added and left at -20 degrees C overnight. The precipitated RNA was spun down at 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300 µl of RNase-free water and 35 µl buffer (Promega) 5 µl DTT, 7 µl RNasin and 8 µl DNase were added. The tube was incubated at 37 degrees C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-precipitated with 1/10 volume of 3 M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down and placed in RNase free water. RNA was stored at -80 degrees C.

The above detailed procedures were carried out to obtain the taqman profiles of the clones in question.

Given below are the Primers and the Taqman results for the following clones:

58092213.0.36 – Probe Name: Ag809 (Table 9 and Table 10)

29692275.0.1 – Probe Name: Ag2773 (Table 11 and Table 12)

32125243.0.21 – Probe Name: Ag427 (Table 13 and Table 14)

27455183.0.19 – Probe Name: Ag1541 (Table 15 and Table 16, 17, 18)

Table 8: Primer Design for Probe Ag809 (FCTR1)

Primer	Sequences	TM	Length	Start Po	SEQID NO
Forward	5'-ATGTGATCTTTGGCTGTGAAGT-3'	58.7	22	337	24
Probe	FAM-5'-CTACCCCATGGCCTCCATCGAGT-3'-TAMRA	69.4	23	365	25
Reverse		59.9	19	393	26

TABLE 9: TAQMAN RESULTS FOR FCTR1

Tissue_Name	Panel 1	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	79.6	Normal Colon GENPAK 061003	6.8	93768_Secondary Th1_anti-CD28/anti-CD3	2.0
Heart (fetal)	43.8	83219 CC Well to Mod Diff (ODO3866)	6.1	93769_Secondary Th2_anti-CD28/anti-CD3	1.5
Pancreas	2.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	2.5
Pancreatic ca. CAPAN 2	4.7	83221 CC Gr.2 rectosigmoid (ODO3868)	0.9	93573_Secondary Th1_resting day 4-6 in IL-2	1.0
Adrenal gland	2.3	83222 CC NAT (ODO3868)	1.2	93572_Secondary Th2_resting day 4-6 in IL-2	3.0
Thyroid	6.5	83235 CC Mod Diff (ODO3920)	3.8	93571_Secondary Tr1_resting day 4-6 in IL-2	1.7
Salivary gland	12.3	83236 CC NAT (ODO3920)	1.3	93568_primary Th1_anti-CD28/anti-CD3	0.4
Pituitary gland	8.7	83237 CC Gr.2 ascend colon (ODO3921)	6.9	93569_primary Th2_anti-CD28/anti-CD3	1.5
Brain (fetal)	0.0	83238 CC NAT (ODO3921)	4.0	93570_primary Tr1_anti-CD28/anti-CD3	2.0
Brain (whole)	3.0	83241 CC from Partial Hepatectomy (ODO4309)	1.2	93565_primary Th1_resting dy 4-6 in IL-2	5.4
Brain (amygdala)	2.4	83242 Liver NAT (ODO4309)	0.6	93566_primary Th2_resting dy 4-6 in IL-2	3.1
Brain (cerebellum)	0.0	87472 Colon mets to lung (OD04451-01)	4.4	93567_primary Tr1_resting dy 4-6 in IL-2	0.0
Brain (hippocampus)	13.0	87473 Lung NAT (OD04451-02)	1.2	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	11.2
Brain (thalamus)	3.0	Normal Prostate Clontech A+ 6546-1	10.2	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	1.2
Cerebral Cortex	2.3	84140 Prostate Cancer (OD04410)	41.8	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.9
Spinal cord	2.6	84141 Prostate NAT (OD04410)	25.7	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0
CNS ca. (glio/astro) U87-MG	12.1	87073 Prostate Cancer (OD04720-01)	11.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.6
CNS ca. (glio/astro) U-118-MG	100.0	87074 Prostate NAT (OD04720-02)	10.0	93354_CD4_none	1.1
CNS ca. (astro) SW1783	6.5	Normal Lung GENPAK 061010	7.9	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0
CNS ca.* (neuro; met) SK-N-AS	52.1	83239 Lung Met to Muscle	6.5	93103_LAK cells_resting	0.5

		(ODO4286)			
CNS ca. (astro) SF-539	12.6	83240 Muscle NAT (ODO4286)	2.6	93788_LAK cells_IL-2	0.0
CNS ca. (astro) SNB-75	11.9	84136 Lung Malignant Cancer (OD03126)	14.8	93787_LAK cells_IL-2+IL-12	0.7
CNS ca. (glio)SNB-19	0.0	84137 Lung NAT (OD03126)	3.2	93789_LAK cells_IL-2+IFN gamma	1.1
CNS ca. (glio)U251	0.9	84871 Lung Cancer (OD04404)	2.1	93790_LAK cells_IL-2+ IL-18	0.3
CNS ca. (glio) SF-295	12.6	84872 Lung NAT (OD04404)	1.9	93104_LAK cells_PMA/ionomycin and IL-18	0.0
Heart	13.9	84875 Lung Cancer (OD04565)	0.3	93578_NK Cells IL-2_resting	1.3
Skeletal muscle	3.2	85950 Lung Cancer (OD04237-01)	1.3	93109_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Bone marrow	3.6	85970 Lung NAT (OD04237-02)	2.6	93110_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Thymus	4.2	83255 Ocular Mel Met to Liver (ODO4310)	0.1	93111_Mixed Lymphocyte Reaction_Two Way MLR	2.7
Spleen	61.6	83256 Liver NAT (ODO4310)	0.6	93112_Mononuclear Cells (PBMCs)_resting	0.0
Lymph node	3.3	84139 Melanoma Mets to Lung (OD04321)	2.5	93113_Mononuclear Cells (PBMCs)_PWM	1.3
Colorectal	11.9	84138 Lung NAT (OD04321)	2.6	93114_Mononuclear Cells (PBMCs)_PHA-L	1.0
Stomach	28.3	Normal Kidney GENPAK 061008	5.6	93249_Ramos (B cell)_none	1.2
Small intestine	4.5	83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.6	93250_Ramos (B cell)_ionomycin	2.3
Colon ca. SW480	46.7	83787 Kidney NAT (OD04338)	3.7	93349_B lymphocytes_PWM	4.3
Colon ca.* (SW480 met)SW620	19.0	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.8	93350_B lymphocytes_CD40L and IL-4	1.4
Colon ca. HT29	5.3	83789 Kidney NAT (OD04339)	3.1	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	7.2
Colon ca. HCT- 116	5.0	83790 Kidney Ca, Clear cell type (OD04340)	1.5	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionom ycin	3.0
Colon ca. CaCo-2	49.3	83791 Kidney NAT (OD04340)	5.1	93356_Dendritic Cells_none	1.5
83219 CC Well to Mod Diff (ODO3866)	3.0	83792 Kidney Ca, Nuclear grade 3 (OD04348)	14.5	93355_Dendritic Cells_LPS 100 ng/ml	0.7
Colon ca. HCC- 2998	27.7	83793 Kidney NAT (OD04348)	2.5	93775_Dendritic Cells_anti-CD40	0.5
Gastric ca.* (liver met) NCI-N87	10.5	87474 Kidney Cancer	1.7	93774_Monocytes_resting	0.5

		(OD04622-01)			
Bladder	3.7	87475 Kidney NAT (OD04622-03)	2.0	93776_Monocytes_LPS 50 ng/ml	0.0
Trachea	23.5	85973 Kidney Cancer (OD04450-01)	0.3	93581_Macrophages_resting	1.3
Kidney	1.8	85974 Kidney NAT (OD04450-03)	2.0	93582_Macrophages_LPS 100 ng/ml	1.8
Kidney (fetal)	1.9	Kidney Cancer Clontech 8120607	7.0	93098_HUVEC (Endothelial)_none	2.3
Renal ca. 786-0	7.0	Kidney NAT Clontech 8120608	1.5	93099_HUVEC (Endothelial)_starved	9.0
Renal ca. A498	6.8	Kidney Cancer Clontech 8120613	2.0	93100_HUVEC (Endothelial)_IL-1b	1.2
Renal ca.RXF 393	4.7	Kidney NAT Clontech 8120614	4.1	93779_HUVEC (Endothelial)_IFN gamma	1.4
Renal ca.ACHN	9.8	Kidney Cancer Clontech 9010320	2.2	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.8
Renal ca.UO-31	1.3	Kidney NAT Clontech 9010321	3.5	93101_HUVEC (Endothelial)_TNF alpha + IL4	1.1
Renal ca.TK-10	0.6	Normal Uterus GENPAK 061018	3.1	93781_HUVEC (Endothelial)_IL-11	3.0
Liver	0.8	Uterus Cancer GENPAK 064011	17.6	93583_Lung Microvascular Endothelial Cells_none	0.8
Liver (fetal)	1.1	Normal Thyroid Clontech A+ 6570-1	3.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Liver ca. (hepatoblast) HepG2	54.0	Thyroid Cancer GENPAK 064010	1.2	92662_Microvascular Dermal endothelium_none	1.1
Lung	3.9	Thyroid Cancer INVITROGEN A302152	0.6	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.0
Lung (fetal)	9.0	Thyroid NAT INVITROGEN A302153	2.6	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0
Lung ca. (small cell) LX-1	34.4	Normal Breast GENPAK 061019	3.4	93347_Small Airway Epithelium_none	0.4
Lung ca. (small cell) NCI-H69	3.0	84877 Breast Cancer (OD04566)	0.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Lung ca. (s.cell var.) SHP-77	13.0	85975 Breast Cancer (OD04590-01)	67.8	92668_Coronary Artery SMC_resting	5.8
Lung ca. (large cell)NCI-H460	6.8	85976 Breast Cancer Mets (OD04590-03)	51.1	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.3
Lung ca. (non-sm. cell) A549	3.4	87070 Breast Cancer Metastasis	12.7	93107_astrocytes_resting	2.7

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		(OD04655-05)			
Lung ca. (non-s.cell) NCI-H23	34.4	GENPAK Breast Cancer 064006	8.9	93108_astrosar TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0
Lung ca (non-s.cell) HOP-62	10.5	Breast Cancer Clontech 9100266	6.2	92666_KU-812 (Basophil)_resting	6.8
Lung ca. (non-s.cl) NCI-H522	47.6	Breast NAT Clontech 9100265	3.3	92667_KU-812 (Basophil)_PMA/ionoycin	8.4
Lung ca. (squam.) SW 900	4.7	Breast Cancer INVITROGEN A209073	3.4	93579_CCD1106 (Keratinocytes)_none	1.6
Lung ca. (squam.) NCI-H596	0.7	Breast NAT INVITROGEN A2090734	8.7	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	1.4
Mammary gland	9.9	Normal Liver GENPAK 061009	1.1	93791_Liver Cirrhosis	4.2
Breast ca.* (pl. effusion) MCF-7	5.6	Liver Cancer GENPAK 064003	0.6	93792_Lupus Kidney	1.9
Breast ca.* (pl.ef) MDA-MB-231	21.3	Liver Cancer Research Genetics RNA 1025	0.6	93577_NCI-H292	39.5
Breast ca.* (pl. effusion) T47D	66.0	Liver Cancer Research Genetics RNA 1026	1.4	93358_NCI-H292_IL-4	39.0
Breast ca. BT-549	7.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	1.3	93360_NCI-H292_IL-9	65.5
Breast ca.MDA-N	18.7	Paired Liver Tissue Research Genetics RNA 6004-N	1.3	93359_NCI-H292_IL-13	37.1
Ovary	12.1	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	1.1	93357_NCI-H292_IFN gamma	31.9
Ovarian ca.OVCAR-3	3.5	Paired Liver Tissue Research Genetics RNA 6005-N	0.3	93777_HPAEC_-	0.5
Ovarian ca.OVCAR-4	4.0	Normal Bladder GENPAK 061001	5.9	93778_HPAEC_IL-1 beta/TNA alpha	1.2
Ovarian ca. OVCAR-5	9.1	Bladder Cancer Research Genetics RNA 1023	1.7	93254_Normal Human Lung Fibroblast_none	42.3
Ovarian ca. OVCAR-8	12.7	Bladder Cancer INVITROGEN A302173	1.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	17.8
Ovarian ca.IGROV-1	9.8	87071 Bladder Cancer (OD04718-01)	2.0	93257_Normal Human Lung Fibroblast_IL-4	100.0
Ovarian ca.*	0.4	87072 Bladder	3.3	93256 Normal Human Lung	72.7

(ascites) SK-OV-3		Normal Adjacent (OD04718-03)		Fibroblast_	
Uterus	6.9	Normal Ovary Res. Gen.	2.2	93255_Normal Human Lung Fibroblast_IL-13	60.7
Placenta	4.6	Ovarian Cancer GENPAK 064008	29.1	93258_Normal Human Lung Fibroblast_IFN gamma	81.8
Prostate	15.7	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	76.8
Prostate ca.* (bone met)PC-3	35.9	87493 Ovary NAT (OD04768-08)	2.2	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	30.2
Testis	14.6	Normal Stomach GENPAK 061017	13.1	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	38.2
Melanoma Hs688(A).T	13.5	NAT Stomach Clontech 9060359	8.8	93772_dermal fibroblast_IFN gamma	34.2
Melanoma* (met) Hs688(B).T	71.2	Gastric Cancer Clontech 9060395	2.5	93771_dermal fibroblast_IL-4	80.7
Melanoma UACC-62	1.7	NAT Stomach Clontech 9060394	9.7	93259_IBD Colitis 1**	0.0
Melanoma M14	9.5	Gastric Cancer Clontech 9060397	15.9	93260_IBD Colitis 2	0.3
Melanoma LOX IMVI	2.4	NAT Stomach Clontech 9060396	12.9	93261_IBD Crohns	1.4
Melanoma* (met)SK-MEL-5	3.4	Gastric Cancer GENPAK 064005	12.1	735010_Colon_normal	35.6
Adipose	5.9			735019_Lung_none	11.0
				64028-1_Thymus_none	5.8
				64030-1_Kidney_none	9.7

Taqman results shown in Table 9 demonstrates that cFCTR1 is highly expressed by tumor cell lines and also overexpressed in tumor tissues, specifically breast and ovarian tumor compared to Normal Adjacent Tissues (NAT). There are reports that follistatin can act as a modulator of tumor growth and its expression also correlate with polycystic ovary syndrome, a benign form of ovarian tumor.

Table 10: Primer Design for Probe Ag2773 (FCTR4)

Primer	Sequences	TM	Length	Start Po	SEQ ID NO
Forward	5'-CCTTGCTTTGTCATATGCTGTT-3'	59.3	22	243	29
Probe	FAM-5'-CCCTTTCCTGGAATATAAACTCTCA-3'-TAMRA	64.6	26	265	30
Reverse	5'-AGAGGAAGCTTCTGGAGAAGA-3'	58.9	22	313	31

TABLE 11: TAQMAN RESULTS FOR CONE FCTR4

Tissue_Name	Panel 1D	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	18.3	Normal Colon GENPAK 061003	41.2	93768_Secondary Th1_anti-CD28/anti-CD3	12.7
Heart (fetal)	4.3	83219 CC Well to Mod Diff (ODO3866)	5.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.2
Pancreas	3.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	14.7
Pancreatic ca.CAPAN 2	20.0	83221 CC Gr.2 rectosigmoid (ODO3868)	0.7	93573_Secondary Th1_resting day 4-6 in IL-2	4.7
Adrenal gland	7.4	83222 CC NAT (ODO3868)	1.4	93572_Secondary Th2_resting day 4-6 in IL-2	3.5
Thyroid	6.8	83235 CC Mod Diff (ODO3920)	14.0	93571_Secondary Tr1_resting day 4-6 in IL-2	7.0
Salivary gland	2.5	83236 CC NAT (ODO3920)	13.9	93568_primary Th1_anti-CD28/anti-CD3	22.4
Pituitary gland	5.7	83237 CC Gr.2 ascend colon (ODO3921)	16.2	93569_primary Th2_anti-CD28/anti-CD3	16.3
Brain (fetal)	14.4	83238 CC NAT (ODO3921)	5.2	93570_primary Tr1_anti-CD28/anti-CD3	21.8
Brain (whole)	19.6	83241 CC from Partial Hepatectomy (ODO4309)	13.9	93565_primary Th1_resting dy 4-6 in IL-2	30.2
Brain (amygdala)	3.7	83242 Liver NAT (ODO4309)	12.7	93566_primary Th2_resting dy 4-6 in IL-2	14.4
Brain (cerebellum)	2.1	87472 Colon mets to lung (OD04451-01)	3.4	93567_primary Tr1_resting dy 4-6 in IL-2	7.4
Brain (hippocampus)	22.7	87473 Lung NAT (OD04451-02)	1.5	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	7.6
Brain (thalamus)	7.4	Normal Prostate Clontech A+ 6546-1	1.0	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	11.1
Cerebral Cortex	47.3	84140 Prostate Cancer (OD04410)	3.1	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.6
Spinal cord	8.3	84141 Prostate NAT (OD04410)	10.6	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	9.7
CNS ca. (glio/astro)U87-MG	19.9	87073 Prostate Cancer (OD04720-01)	9.7	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	6.2
CNS ca. (glio/astro) U-118-MG	57.0	87074 Prostate NAT (OD04720-02)	8.3	93354_CD4_none	6.4
CNS ca. (astro) SW1783	10.0	Normal Lung GENPAK 061010	36.6	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	9.3
CNS ca.* (neuro; met)SK-N-AS	44.8	83239 Lung Met to Muscle (ODO4286)	11.7	93103_LAK cells_resting	11.0
CNS ca. (astro) SF-539	37.4	83240 Muscle NAT (ODO4286)	3.4	93788_LAK cells_IL-2	10.4
CNS ca. (astro) SNB-75	62.0	84136 Lung Malignant Cancer (OD03126)	15.1	93787_LAK cells_IL-2+IL-12	7.4

CNS ca. (glio) SNB-19	24.8	84137 Lung NAT (OD03126)	17.4	93789_LAK cells_IL-2+IFN gamma	11.6
CNS ca. (glio) U251	40.3	84871 Lung Cancer (OD04404)	5.0	93790_LAK cells_IL-2+ IL-18	13.3
CNS ca. (glio) SF-295	100.0	84872 Lung NAT (OD04404)	6.3	93104_LAK cells_PMA/ionomycin and IL-18	4.8
Heart	0.0	84875 Lung Cancer (OD04565)	3.2	93578_NK Cells IL-2_resting	6.2
Skeletal muscle	0.0	85950 Lung Cancer (OD04237-01)	15.8	93109_Mixed Lymphocyte Reaction_Two Way MLR	12.3
Bone marrow	33.7	85970 Lung NAT (OD04237-02)	10.5	93110_Mixed Lymphocyte Reaction_Two Way MLR	8.7
Thymus	12.4	83255 Ocular Mel Met to Liver (ODO4310)	5.9	93111_Mixed Lymphocyte Reaction_Two Way MLR	3.5
Spleen	21.3	83256 Liver NAT (ODO4310)	3.6	93112_Mononuclear Cells (PBMcs)_resting	4.5
Lymph node	13.4	84139 Melanoma Mets to Lung (OD04321)	10.6	93113_Mononuclear Cells (PBMcs)_PWM	21.2
Colorectal	38.2	84138 Lung NAT (OD04321)	10.6	93114_Mononuclear Cells (PBMcs)_PHA-L	8.9
Stomach	9.9	Normal Kidney GENPAK 061008	26.2	93249_Ramos (B cell)_none	100.0
Small intestine	17.9	83786 Kidney Ca, Nuclear grade 2 (OD04338)	22.2	93250_Ramos (B cell)_ionomycin	28.7
Colon ca.SW480	27.7	83787 Kidney NAT (OD04338)	11.7	93349_B lymphocytes_PWM	20.0
Colon ca.* (SW480 met)SW620	30.8	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	45.1	93350_B lymphocytes_CD40L and IL- 4	7.8
Colon ca.HT29	8.1	83789 Kidney NAT (OD04339)	14.8	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	8.0
Colon ca.HCT- 116	35.4	83790 Kidney Ca, Clear cell type (OD04340)	26.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	3.8
Colon ca. CaCo- 2	37.6	83791 Kidney NAT (OD04340)	10.4	93356_Dendritic Cells_none	6.8
83219 CC Well to Mod Diff (ODO3866)	17.8	83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.4	93355_Dendritic Cells_LPS 100 ng/ml	3.3
Colon ca.HCC- 2998	19.9	83793 Kidney NAT (OD04348)	18.8	93775_Dendritic Cells_anti-CD40	6.3
Gastric ca.* (liver met) NCI- N87	73.2	87474 Kidney Cancer (OD04622-01)	5.6	93774_Monocytes_resting	10.6
Bladder	43.2	87475 Kidney NAT (OD04622- 03)	0.5	93776_Monocytes_LPS 50 ng/ml	3.5
Trachea	10.3	85973 Kidney Cancer (OD04450-01)	21.2	93581_Macrophages_resting	7.6
Kidney	9.2	85974 Kidney NAT (OD04450- 03)	9.3	93582_Macrophages_LPS 100 ng/ml	3.9

Kidney (fetal)	0.0	Kidney Cancer Clontech 8120607	0.0	93098_HUVEC (Endothelial)_none	8.5
Renal ca.786-0	53.6	Kidney NAT Clontech 8120608	0.9	93099_HUVEC (Endothelial)_starved	17.9
Renal ca. A498	36.1	Kidney Cancer Clontech 8120613	0.0	93100_HUVEC (Endothelial)_IL-1b	6.0
Renal ca.RXF 393	31.6	Kidney NAT Clontech 8120614	0.9	93779_HUVEC (Endothelial)_IFN gamma	7.8
Renal ca.ACHN	21.6	Kidney Cancer Clontech 9010320	2.7	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	5.7
Renal ca.UO-31	28.7	Kidney NAT Clontech 9010321	5.0	93101_HUVEC (Endothelial)_TNF alpha + IL4	5.6
Renal ca.TK-10	7.0	Normal Uterus GENPAK 061018	5.3	93781_HUVEC (Endothelial)_IL-11	4.9
Liver	14.2	Uterus Cancer GENPAK 064011	9.0	93583_Lung Microvascular Endothelial Cells_none	4.9
Liver (fetal)	14.5	Normal Thyroid Clontech A+ 6570-1	3.4	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	4.9
Liver ca. (hepatoblast) HepG2	59.9	Thyroid Cancer GENPAK 064010	1.8	92662_Microvascular Dermal endothelium_none	8.6
Lung	17.8	Thyroid Cancer INVITROGEN A302152	3.6	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	6.0
Lung (fetal)	9.6	Thyroid NAT INVITROGEN A302153	4.9	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.9
Lung ca. (small cell) LX-1	70.2	Normal Breast GENPAK 061019	8.5	93347_Small Airway Epithelium_none	1.3
Lung ca. (small cell) NCI-H69	29.9	84877 Breast Cancer (OD04566)	1.5	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	13.2
Lung ca. (s.cell var.) SHP-77	3.9	85975 Breast Cancer (OD04590-01)	23.8	92668_Coronary Artery SMC_resting	3.4
Lung ca. (large cell)NCI-H460	2.0	85976 Breast Cancer Mets (OD04590-03)	24.5	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.0
Lung ca. (non- sm. cell) A549	28.5	87070 Breast Cancer Metastasis (OD04655-05)	12.9	93107_astrocytes_resting	4.7
Lung ca. (non- s.cell) NCI-H23	36.1	GENPAK Breast Cancer 064006	11.8	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.9
Lung ca (non- s.cell) HOP-62	29.9	Breast Cancer Clontech 9100266	3.2	92666_KU-812 (Basophil)_resting	5.8
Lung ca. (non- s.cl) NCI-H522	17.2	Breast NAT Clontech 9100265	1.8	92667_KU-812 (Basophil)_PMA/ionoycin	12.0
Lung ca. (squam.) SW 900	63.7	Breast Cancer INVITROGEN A209073	11.0	93579_CCD1106 (Keratinocytes)_none	4.9
Lung ca.	10.0	Breast NAT	7.1	93580_CCD1106	0.3

(squam.) NCI-H596		INVITROGEN 90734		(Keratinocyte TNFa and IFNg **	
Mammary gland	4.6	Normal Liver GENPAK 061009	8.8	93791_Liver Cirrhosis	1.8
Breast ca.* (pl. effusion) MCF-7	0.0	Liver Cancer GENPAK 064003	4.9	93792_Lupus Kidney	1.6
Breast ca.* (pl.ef) MDA-MB-231	38.7	Liver Cancer Research Genetics RNA 1025	1.0	93577_NCI-H292	11.1
Breast ca.* (pl. effusion) T47D	0.0	Liver Cancer Research Genetics RNA 1026	0.8	93358_NCI-H292_IL-4	12.2
Breast ca.BT-549	4.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.0	93360_NCI-H292_IL-9	7.6
Breast ca.MDA-N	19.0	Paired Liver Tissue Research Genetics RNA 6004-N	7.3	93359_NCI-H292_IL-13	6.1
Ovary	1.7	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.2	93357_NCI-H292_IFN gamma	5.8
Ovarian ca.OVCAR-3	4.8	Paired Liver Tissue Research Genetics RNA 6005-N	0.0	93777_HPAEC_-	6.8
Ovarian ca.OVCAR-4	0.0	Normal Bladder GENPAK 061001	19.8	93778_HPAEC_IL-1 beta/TNA alpha	5.4
Ovarian ca.OVCAR-5	39.0	Bladder Cancer Research Genetics RNA 1023	3.1	93254_Normal Human Lung Fibroblast_none	2.1
Ovarian ca.OVCAR-8	36.6	Bladder Cancer INVITROGEN A302173	9.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	1.9
Ovarian ca.IGROV-1	0.0	87071 Bladder Cancer (OD04718-01)	6.6	93257_Normal Human Lung Fibroblast_IL-4	3.6
Ovarian ca.* (ascites) SK-OV-3	65.5	87072 Bladder Normal Adjacent (OD04718-03)	4.0	93256_Normal Human Lung Fibroblast_IL-9	3.3
Uterus	1.6	Normal Ovary Res. Gen.	0.3	93255_Normal Human Lung Fibroblast_IL-13	2.3
Placenta	8.9	Ovarian Cancer GENPAK 064008	6.8	93258_Normal Human Lung Fibroblast_IFN gamma	2.9
Prostate	0.0	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	5.6
Prostate ca.* (bone met)PC-3	9.2	87493 Ovary NAT (OD04768-08)	3.6	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	17.4
Testis	29.5	Normal Stomach GENPAK 061017	8.6	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	3.8
Melanoma	14.3	NAT Stomach	0.7	93772_dermal fibroblast_IFN gamma	2.6

Hs688(A).T		Clontech 9060359			
Melanoma* (met) Hs688(B).T	22.9	Gastric Cancer Clontech 9060395	3.9	93771_dermal fibroblast_IL-4	3.4
Melanoma UACC-62	9.7	NAT Stomach Clontech 9060394	5.3	93259_IBD Colitis 1**	0.2
Melanoma M14	12.7	Gastric Cancer Clontech 9060397	13.2	93260_IBD Colitis 2	0.4
Melanoma LOX IMVI	4.5	NAT Stomach Clontech 9060396	1.1	93261_IBD Crohns	0.3
Melanoma* (met) SK-MEL-5	21.8	Gastric Cancer GENPAK 064005	23.0	735010_Colon_normal	3.3
Adipose	6.7			735019_Lung_none	3.9
				64028-1_Thymus_none	7.7
				64030-1_Kidney_none	21.8

Table 12 shows the taqman results of clone FCTR4 indicating overexpression in ovarian cancer as compared to Normal Adjacent Tissue (NAT). In addition, increased expression is demonstrated by ovarian tumor cell line suggesting that antibodies could be used to treat ovarian tumors.

5

Table 13: Primer Design for Probe Ag427 (FCTR5)

Primer	Sequences	Length	Start Po	SEQ ID NO
Forward	5'-GAGCTACAGGCAGCCTCGAGT-3'	21	443	32
Probe	TET-5'-TGGCCCAGCTGACCCTGCTCA-3'-TAMRA	21		33
Reverse	5'-GGCTACGTCAGTGGGTTTGG-3'	20	449	34

Table 14: Taqman results for FCTR5

Tissue_Name	Panel 1	Tissue_Name	Panel 4D
Endothelial cells	10.7	93768_Secondary Th1_anti-CD28/anti-CD3	15.9
Endothelial cells (treated)	15.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.7
Pancreas	16.2	93770_Secondary Tr1_anti-CD28/anti-CD3	21.9
Pancreatic ca.CAPAN 2	10.5	93573_Secondary Th1_resting day 4-6 in IL-2	12.3
Adipose	45.1	93572_Secondary Th2_resting day 4-6 in IL-2	16.2
Adrenal gland	61.6	93571_Secondary Tr1_resting day 4-6 in IL-2	16.2
Thyroid	13.1	93568_primary Th1_anti-CD28/anti-CD3	13.9

Salivary gland	33.7	93569_primary Th2_anti-CD28/anti-CD3	14.6
Pituitary gland	15.8	93570_primary Tr1_anti-CD28/anti-CD3	26.2
Brain (fetal)	7.2	93565_primary Th1_resting dy 4-6 in IL-2	56.3
Brain (whole)	6.3	93566_primary Th2_resting dy 4-6 in IL-2	27.7
Brain (amygdala)	8.4	93567_primary Tr1_resting dy 4-6 in IL-2	31.6
Brain (cerebellum)	6.8	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	12.1
Brain (hippocampus)	7.9	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	17.1
Brain (substantia nigra)	9.5	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.1
Brain (thalamus)	7.9	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	13.4
Brain (hypothalamus)	23.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	9.2
Spinal cord	9.5	93354_CD4_none	7.6
CNS ca. (glio/astro)U87-MG	12.6	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	20.2
CNS ca. (glio/astro)U-118-MG	11.6	93103_LAK cells_resting	57.0
CNS ca. (astro)SW1783	4.3	93788_LAK cells_IL-2	18.8
CNS ca.* (neuro; met)SK-N-AS	10.4	93787_LAK cells_IL-2+IL-12	14.2
CNS ca. (astro) SF-539	11.6	93789_LAK cells_IL-2+IFN gamma	20.9
CNS ca. (astro) SNB-75	4.4	93790_LAK cells_IL-2+ IL-18	14.8
CNS ca. (glio)SNB-19	31.6	93104_LAK cells_PMA/ionomycin and IL-18	12.9
CNS ca. (glio)U251	17.3	93578_NK Cells IL-2_resting	17.4
CNS ca. (glio)SF-295	20.9	93109_Mixed Lymphocyte Reaction_Two Way MLR	43.5
Heart	14.3	93110_Mixed Lymphocyte Reaction_Two Way MLR	19.3
Skeletal muscle	11.7	93111_Mixed Lymphocyte Reaction_Two Way MLR	12.6
Bone marrow	21.9	93112_Mononuclear Cells (PBMCs)_resting	8.7
Thymus	20.9	93113_Mononuclear Cells (PBMCs)_PWM	28.5
Spleen	23.8	93114_Mononuclear Cells (PBMCs)_PHA-L	26.2
Lymph node	24.2	93249_Ramos (B cell)_none	0.3
Colon (ascending)	17.2	93250_Ramos (B cell)_ionomycin	1.2
Stomach	11.1	93349_B lymphocytes_PWM	25.7
Small intestine	21.5	93350_B lymphocytes_CD40L and IL-4	13.0
Colon ca.SW480	12.2	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	26.4
Colon ca.* (SW480 met)SW620	8.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	11.4
Colon ca.HT29	16.2	93356_Dendritic Cells_none	40.3
Colon ca.HCT-116	8.1	93355_Dendritic Cells_LPS 100 ng/ml	33.0
Colon ca.CaCo-2	22.1	93775_Dendritic Cells_anti-CD40	20.5
Colon ca.HCT-15	18.6	93774_Monocytes_resting	23.3
Colon ca.HCC-2998	21.9	93776_Monocytes_LPS 50 ng/ml	6.9
Gastric ca.* (liver met) NCI-N87	42.9	93581_Macrophages_resting	14.7
Bladder	95.3	93582_Macrophages_LPS 100 ng/ml	64.6
Trachea	18.3	93098_HUVEC (Endothelial)_none	6.8
Kidney	25.7	93099_HUVEC (Endothelial)_starved	13.9
Kidney (fetal)	15.8	93100_HUVEC (Endothelial)_IL-1b	7.5
Renal ca.786-0	16.5	93779_HUVEC (Endothelial)_IFN gamma	27.7
Renal ca.A498	16.5	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	11.8
Renal ca.RXF 393	7.4	93101_HUVEC (Endothelial)_TNF alpha + IL4	6.7

Renal ca.ACHN	11.9	93781_HUVEC (Endothelial Cells)_IL-11	10.4
Renal ca.UO-31	15.8	93583_Lung Microvascular Endothelial Cells_none	8.8
Renal ca.TK-10	28.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	8.6
Liver	100.0	92662_Microvascular Dermal endothelium_none	22.1
Liver (fetal)	81.8	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	18.7
Liver ca. (hepatoblast) HepG2	28.3	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	35.4
Lung	10.7	93347_Small Airway Epithelium_none	10.9
Lung (fetal)	10.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	50.0
Lung ca. (small cell) LX-1	24.3	92668_Coronary Artery SMC_resting	27.9
Lung ca. (small cell) NCI-H69	41.5	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	25.4
Lung ca. (s.cell var.) SHP-77	4.6	93107_astrocytes_resting	7.4
Lung ca. (large cell)NCI-H460	46.3	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	10.7
Lung ca. (non-sm. cell) A549	45.4	92666_KU-812 (Basophil)_resting	3.2
Lung ca. (non-s.cell) NCI-H23	54.3	92667_KU-812 (Basophil)_PMA/ionoycin	6.7
Lung ca (non-s.cell) HOP-62	50.7	93579_CCD1106 (Keratinocytes)_none	12.2
Lung ca. (non-s.cl) NCI-H522	38.4	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	100.0
Lung ca. (squam.) SW 900	30.8	93791_Liver Cirrhosis	27.6
Lung ca. (squam.) NCI-H596	15.5	93792_Lupus Kidney	32.3
Mammary gland	65.5	93577_NCI-H292	77.4
Breast ca.* (pl. effusion) MCF-7	4.4	93358_NCI-H292_IL-4	70.2
Breast ca.* (pl.ef) MDA-MB-231	3.5	93360_NCI-H292_IL-9	54.3
Breast ca.* (pl. effusion)T47D	8.7	93359_NCI-H292_IL-13	47.0
Breast ca. BT-549	5.7	93357_NCI-H292_IFN gamma	52.9
Breast ca.MDA-N	16.6	93777_HPAEC_-	23.8
Ovary	20.5	93778_HPAEC_IL-1 beta/TNA alpha	21.5
Ovarian ca. OVCAR-3	21.6	93254_Normal Human Lung Fibroblast_none	49.3
Ovarian ca.OVCAR-4	8.3	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	40.3
Ovarian ca.OVCAR-5	26.1	93257_Normal Human Lung Fibroblast_IL-4	48.3
Ovarian ca.OVCAR-8	48.0	93256_Normal Human Lung Fibroblast_IL-9	29.3
Ovarian ca.IGROV-1	9.3	93255_Normal Human Lung Fibroblast_IL-13	73.7
Ovarian ca.* (ascites)SK-OV-3	8.8	93258_Normal Human Lung Fibroblast_IFN gamma	66.9
Uterus	13.4	93106_Dermal Fibroblasts CCD1070_resting	20.2
Placenta	9.4	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	35.1
Prostate	21.3	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	15.0
Prostate ca.* (bone met)PC-3	17.7	93772_dermal fibroblast_IFN gamma	21.8
Testis	11.7	93771_dermal fibroblast_IL-4	21.2
Melanoma Hs688(A).T	9.0	93259_IBD Colitis 1**	8.8
Melanoma* (met) Hs688(B).T	12.9	93260_IBD Colitis 2	3.5
Melanoma UACC-62	12.4	93261_IBD Crohns	1.3

Melanoma M14	9.5	735010_Colon_normal	20.3
Melanoma LOX IMVI	8.1	735019_Lung_none	40.3
Melanoma* (met) SK-MEL-3	8.8	64028-1_Thymus_none	33.5
Melanoma SK-MEL-28	8.0	64030-1_Kidney_none	21.0

Taqman results in Table 14 show high expression of clone FCTR5 in bladder, liver and adrenal gland suggesting a possible role in the treatment of diseases involving these tissues.

5 **Table 15: Primer Design for Probe Ag1541 (FCTR6)**

Primer	Sequences	TM	Length	Start Pos.	SEQ ID NO
Forward	5'-AGAAGAACACCCCAGGGATATA-3'	58.8	22	1076	35
Probe	FAM-5'-CCTCGTTGGTGAAC TACAACCTCTGG-3'-TAMRA	67.9	26	1100	36
Reverse	5'-CCTCTAGCTGGGTCAC TTTCTC-3'	59.5	22	1129	37

TABLE 16: TAQMAN RESULTS FOR FCTR6 (PANEL 1D)

Tissue_Name	Panel 1D	
	Run 1	Run 2
Liver adenocarcinoma	0.0	0.0
Heart (fetal)	0.0	0.0
Pancreas	0.0	0.0
Pancreatic ca.CAPAN 2	0.0	0.0
Adrenal gland	0.0	0.0
Thyroid	0.0	0.0
Salivary gland	0.0	0.0
Pituitary gland	0.0	0.0
Brain (fetal)	0.5	0.4
Brain (whole)	1.1	1.7
Brain (amygdala)	0.0	1.8
Brain (cerebellum)	0.6	1.9
Brain (hippocampus)	3.3	3.4
Brain (thalamus)	1.0	1.2
Cerebral Cortex	1.6	2.6
Spinal cord	2.5	0.4
CNS ca. (glio/astro)U87-MG	0.0	0.0
CNS ca. (glio/astro)U-118-MG	0.0	0.0
CNS ca. (astro)SW1783	0.0	0.0
CNS ca.* (neuro; met)SK-N-AS	0.0	0.0
CNS ca. (astro)SF-539	0.0	0.0
CNS ca. (astro) SNB-75	0.7	0.0
CNS ca. (glio)SNB-19	0.0	0.0
CNS ca. (glio)U251	0.0	0.0
CNS ca. (glio)SF-295	0.0	0.8
Heart	0.0	0.0
Skeletal muscle	0.0	0.0

Bone marrow		0.0
Thymus		0.0
Spleen	0.0	0.0
Lymph node	0.0	0.0
Colorectal	0.0	0.6
Stomach	1.9	0.0
Small intestine	0.0	1.0
Colon ca. SW480	0.0	0.0
Colon ca.* (SW480 met)SW620	0.0	0.0
Colon ca. HT29	0.0	0.0
Colon ca. HCT-116	0.6	0.4
Colon ca. CaCo-2	1.5	0.0
83219 CC Well to Mod Diff (ODO3866)	0.0	0.0
Colon ca. HCC-2998	0.0	0.0
Gastric ca.* (liver met) NCI-N87	1.2	0.0
Bladder	0.0	0.0
Trachea	0.0	0.4
Kidney	0.8	1.2
Kidney (fetal)	0.5	0.7
Renal ca. 786-0	0.0	0.0
Renal ca. A498	0.0	0.0
Renal ca. RXF 393	0.0	0.0
Renal ca. ACHN	0.0	0.0
Renal ca. UO-31	0.0	0.0
Renal ca. TK-10	0.0	0.0
Liver	0.0	0.0
Liver (fetal)	0.2	0.0
Liver ca. (hepatoblast) HepG2	0.0	0.0
Lung	0.0	0.0
Lung (fetal)	0.0	0.0
Lung ca. (small cell) LX-1	1.7	2.3
Lung ca. (small cell) NCI-H69	0.0	0.0
Lung ca. (s.cell var.) SHP-77	1.3	2.5
Lung ca. (large cell) NCI-H460	0.0	0.0
Lung ca. (non-sm. cell) A549	0.0	0.0
Lung ca. (non-s.cell) NCI-H23	1.2	0.4
Lung ca. (non-s.cell) HOP-62	0.0	0.0
Lung ca. (non-s.cl) NCI-H522	0.0	0.0
Lung ca. (squam.) SW 900	0.0	0.7
Lung ca. (squam.) NCI-H596	0.0	1.3
Mammary gland	0.0	1.5
Breast ca.* (pl. effusion) MCF-7	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	5.8	0.5
Breast ca.* (pl. effusion) T47D	1.2	0.3
Breast ca. BT-549	0.5	0.0
Breast ca. MDA-N	0.0	0.0
Ovary	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0
Ovarian ca. OVCAR-5	3.6	0.7
Ovarian ca. OVCAR-8	0.0	0.0
Ovarian ca. IGROV-1	0.0	0.0
Ovarian ca.* (ascites) SK-OV-3	0.0	0.0
Uterus	0.0	0.0
Placenta	0.0	0.0
Prostate	0.0	0.7
Prostate ca.* (bone met) PC-3	0.0	0.0
Testis	100.0	100.0
Melanoma Hs688(A).T	0.0	0.0

Melanoma* (met) Hs6894-T	0.0	0.0
Melanoma UACC-62	0.0	0.0
Melanoma M14	0.0	0.0
Melanoma LOX IMVI	0.0	0.0
Melanoma* (met)SK-MEL-5	0.0	0.0
Adipose	0.5	0.0

Table 17: Taqman Results for FCTR6 (Panel 2D)

Tissue_Name	Panel 2D	
	Run 1	Run 2
Normal Colon GENPAK 061003	5.4	2.4
83219 CC Well to Mod Diff (ODO3866)	7.3	0.0
83220 CC NAT (ODO3866)	5.8	1.5
83221 CC Gr.2 rectosigmoid (ODO3868)	3.4	0.0
83222 CC NAT (ODO3868)	0.0	0.0
83235 CC Mod Diff (ODO3920)	11.0	1.4
83236 CC NAT (ODO3920)	0.0	0.0
83237 CC Gr.2 ascend colon (ODO3921)	6.2	2.5
83238 CC NAT (ODO3921)	10.2	0.0
83241 CC from Partial Hepatectomy (ODO4309)	3.6	0.0
83242 Liver NAT (ODO4309)	0.0	2.4
87472 Colon mets to lung (OD04451-01)	7.2	4.4
87473 Lung NAT (OD04451-02)	0.0	0.0
Normal Prostate Clontech A+ 6546-1	4.8	2.9
84140 Prostate Cancer (OD04410)	3.5	0.0
84141 Prostate NAT (OD04410)	3.4	0.0
87073 Prostate Cancer (OD04720-01)	9.0	8.5
87074 Prostate NAT (OD04720-02)	0.0	0.0
Normal Lung GENPAK 061010	17.7	6.5
83239 Lung Met to Muscle (ODO4286)	0.0	2.3
83240 Muscle NAT (ODO4286)	0.0	0.0
84136 Lung Malignant Cancer (OD03126)	6.5	5.7
84137 Lung NAT (OD03126)	0.0	0.0
84871 Lung Cancer (OD04404)	0.0	0.0
84872 Lung NAT (OD04404)	0.0	0.0
84875 Lung Cancer (OD04565)	0.0	0.0
85950 Lung Cancer (OD04237-01)	0.0	0.0
85970 Lung NAT (OD04237-02)	0.0	0.0
83255 Ocular Mel Met to Liver (ODO4310)	4.3	0.0
83256 Liver NAT (ODO4310)	0.0	0.0
84139 Melanoma Mets to Lung (OD04321)	0.0	0.0
84138 Lung NAT (OD04321)	0.0	0.0
Normal Kidney GENPAK 061008	28.1	39.2
83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.0	3.0
83787 Kidney NAT (OD04338)	22.7	31.6
83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	3.1
83789 Kidney NAT (OD04339)	97.3	100.0
83790 Kidney Ca, Clear cell type (OD04340)	0.0	0.0
83791 Kidney NAT (OD04340)	100.0	34.4
83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.0	4.9
83793 Kidney NAT (OD04348)	30.2	19.9
87474 Kidney Cancer (OD04622-01)	0.0	2.4
87475 Kidney NAT (OD04622-03)	8.4	7.2
85973 Kidney Cancer (OD04450-01)	0.0	0.0
85974 Kidney NAT (OD04450-03)	47.3	12.9

Kidney Cancer Clontech 8120607	0.0	0.0
Kidney NAT Clontech 8120608	0.0	0.0
Kidney Cancer Clontech 8120613	0.0	0.0
Kidney NAT Clontech 8120614	20.6	22.9
Kidney Cancer Clontech 9010320	0.0	0.0
Kidney NAT Clontech 9010321	3.4	26.4
Normal Uterus GENPAK 061018	0.0	0.0
Uterus Cancer GENPAK 064011	14.9	0.0
Normal Thyroid Clontech A+ 6570-1	0.0	0.0
Thyroid Cancer GENPAK 064010	0.0	0.0
Thyroid Cancer INVITROGEN A302152	0.0	0.0
Thyroid NAT INVITROGEN A302153	0.0	0.0
Normal Breast GENPAK 061019	5.2	3.5
84877 Breast Cancer (OD04566)	0.0	0.0
85975 Breast Cancer (OD04590-01)	0.0	0.0
85976 Breast Cancer Mets (OD04590-03)	0.0	0.0
87070 Breast Cancer Metastasis (OD04655-05)	0.0	0.0
GENPAK Breast Cancer 064006	0.0	2.5
Breast Cancer Clontech 9100266	6.2	0.0
Breast NAT Clontech 9100265	0.0	0.0
Breast Cancer INVITROGEN A209073	1.5	2.5
Breast NAT INVITROGEN A2090734	24.3	26.2
Normal Liver GENPAK 061009	10.5	2.7
Liver Cancer GENPAK 064003	5.9	1.7
Liver Cancer Research Genetics RNA 1025	21.6	11.0
Liver Cancer Research Genetics RNA 1026	0.0	0.0
Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.3	13.5
Paired Liver Tissue Research Genetics RNA 6004-N	3.2	1.4
Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.0	0.0
Paired Liver Tissue Research Genetics RNA 6005-N	0.0	0.0
Normal Bladder GENPAK 061001	0.0	0.0
Bladder Cancer Research Genetics RNA 1023	0.0	0.0
Bladder Cancer INVITROGEN A302173	4.6	2.3
87071 Bladder Cancer (OD04718-01)	17.9	11.4
87072 Bladder Normal Adjacent (OD04718-03)	0.0	0.0
Normal Ovary Res. Gen.	0.0	0.0
Ovarian Cancer GENPAK 064008	1.7	4.8
87492 Ovary Cancer (OD04768-07)	0.0	2.1
87493 Ovary NAT (OD04768-08)	0.0	0.0
Normal Stomach GENPAK 061017	3.3	2.9
NAT Stomach Clontech 9060359	0.0	0.0
Gastric Cancer Clontech 9060395	0.0	0.0
NAT Stomach Clontech 9060394	0.0	0.0
Gastric Cancer Clontech 9060397	0.0	0.0
NAT Stomach Clontech 9060396	0.0	0.0
Gastric Cancer GENPAK 064005	6.3	3.8

Table 18: Taqman Results for clone 27455183.0.19 (Panel 4D)

Tissue_Name	Panel 4D	
	Run 1	Run 2
93768_Secondary Th1_anti-CD28/anti-CD3	0.0	0.0
93769_Secondary Th2_anti-CD28/anti-CD3	0.0	0.0
93770_Secondary Tr1_anti-CD28/anti-CD3	13.5	17.1
93573_Secondary Th1_resting day 4-6 in IL-2	0.0	0.0
93572_Secondary Th2_resting day 4-6 in IL-2	0.0	0.0

93571_Secondary Tr1_resting day 4-6 in IL-2	0.0	0.0
93568_primary Th1_anti-CD28/anti-CD3	0.0	0.0
93569_primary Th2_anti-CD28/anti-CD3	0.0	0.0
93570_primary Tr1_anti-CD28/anti-CD3	0.0	0.0
93565_primary Th1_resting dy 4-6 in IL-2	0.0	0.0
93566_primary Th2_resting dy 4-6 in IL-2	0.0	0.0
93567_primary Tr1_resting dy 4-6 in IL-2	0.0	0.0
93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.0	0.0
93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0	0.0
93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.0	0.0
93354_CD4_none	5.8	0.0
93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0
93103_LAK cells_resting	0.0	0.0
93788_LAK cells_IL-2	0.0	0.0
93787_LAK cells_IL-2+IL-12	0.0	0.0
93789_LAK cells_IL-2+IFN gamma	0.0	0.0
93790_LAK cells_IL-2+ IL-18	0.0	0.0
93104_LAK cells_PMA/ionomycin and IL-18	0.0	0.0
93578_NK Cells IL-2_resting	0.0	0.0
93109_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93110_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93111_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93112_Mononuclear Cells (PBMCs)_resting	0.0	0.0
93113_Mononuclear Cells (PBMCs)_PWM	0.0	0.0
93114_Mononuclear Cells (PBMCs)_PHA-L	0.0	0.0
93249_Ramos (B cell)_none	0.0	38.2
93250_Ramos (B cell)_ionomycin	0.0	0.0
93349_B lymphocytes_PWM	0.0	68.8
93350_B lymphocytes_CD40L and IL-4	31.0	0.0
92665_EOL-1 (Eosinophil)_dbcAMP differentiated	0.0	0.0
93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	0.0	0.0
93356_Dendritic Cells_none	0.0	0.0
93355_Dendritic Cells_LPS 100 ng/ml	0.0	0.0
93775_Dendritic Cells_anti-CD40	32.5	0.0
93774_Monocytes_resting	0.0	0.0
93776_Monocytes_LPS 50 ng/ml	0.0	0.0
93581_Macrophages_resting	0.0	0.0
93582_Macrophages_LPS 100 ng/ml	0.0	0.0
93098_HUVEC (Endothelial)_none	0.0	0.0
93099_HUVEC (Endothelial)_starved	11.3	0.0
93100_HUVEC (Endothelial)_IL-1b	0.0	14.6
93779_HUVEC (Endothelial)_IFN gamma	0.0	0.0
93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.0	0.0
93101_HUVEC (Endothelial)_TNF alpha + IL4	0.0	0.0
93781_HUVEC (Endothelial)_IL-11	0.0	0.0
93583_Lung Microvascular Endothelial Cells_none	0.0	0.0
93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92662_Microvascular Dermal endothelium_none	0.0	0.0
92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0	0.0
93347_Small Airway Epithelium_none	0.0	0.0
93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92668_Coronary Artery SMC_resting	0.0	0.0
92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93107_astrocytes_resting	0.0	0.0

93108_astrocytes_TNF (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92666_KU-812 (Basophil) _resting	0.0	40.3
92667_KU-812 (Basophil) _PMA/ionoycin	0.0	0.0
93579_CCD1106 (Keratinocytes) _none	0.0	0.0
93580_CCD1106 (Keratinocytes) _TNFa and IFNg **	0.0	0.0
93791_Liver Cirrhosis	100.0	99.3
93792_Lupus Kidney	0.0	0.0
93577_NCI-H292	0.0	0.0
93358_NCI-H292_IL-4	0.0	0.0
93360_NCI-H292_IL-9	10.6	0.0
93359_NCI-H292_IL-13	0.0	65.5
93357_NCI-H292_IFN gamma	0.0	24.8
93777_HPAEC _	0.0	0.0
93778_HPAEC_IL-1 beta/TNA alpha	0.0	0.0
93254_Normal Human Lung Fibroblast _none	0.0	0.0
93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	0.0	0.0
93257_Normal Human Lung Fibroblast_IL-4	0.0	0.0
93256_Normal Human Lung Fibroblast_IL-9	0.0	0.0
93255_Normal Human Lung Fibroblast_IL-13	0.0	0.0
93258_Normal Human Lung Fibroblast_IFN gamma	0.0	0.0
93106_Dermal Fibroblasts CCD1070 _resting	0.0	0.0
93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	0.0	43.8
93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	0.0	0.0
93772_dermal fibroblast_IFN gamma	42.0	27.7
93771_dermal fibroblast_IL-4	10.7	90.1
93259_IBD Colitis 1**	0.0	0.0
93260_IBD Colitis 2	13.8	0.0
93261_IBD Crohns	0.0	46.7
735010_Colon _normal	15.6	0.0
735019_Lung _none	12.9	16.8
64028-1_Thymus _none	69.3	100.0
64030-1_Kidney _none	0.0	0.0

Taqman results in Table 18 demonstrate that clone FCTR6 is differentially expressed in clear cell Renal cell carcinoma tissues versus the normal adjacent kidney tissues and thus could have a potential role in the treatment of renal cell carcinoma.

EQUIVALENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims which follow. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described

herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims.

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